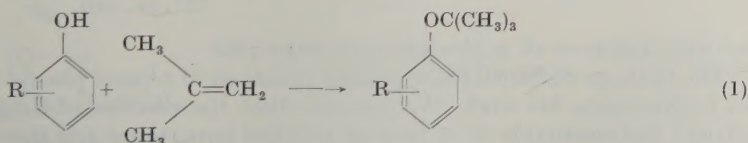


Studies on peroxy compounds

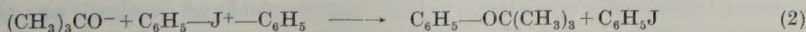
XII.¹ Preparation and dealkylation of *t*-butyl aryl ethers

By SVEN-OLOV LAWESSON and CHRISTER FRISELL

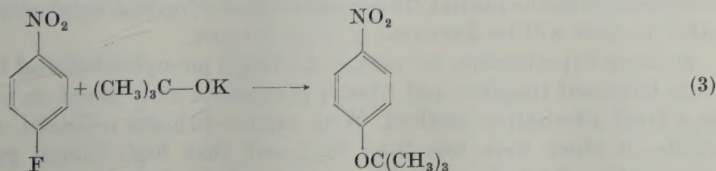
The first attempt to prepare a *t*-butyl aryl ether was, to our knowledge, made by Smith [1] in 1933, who claimed to have synthesized *t*-butyl phenyl ether by reacting sodium phenolate in alcohol with *t*-butyl bromide. The product was said to consist of colourless crystals, no accurate melting point could be determined, the yield was low and on reflux it mostly rearranged to *p*-*t*-butyl phenol. In recent books of theoretical organic chemistry, this last statement on the thermally rearrangement of *t*-butyl phenyl ether is often quoted [2, 3]. As aliphatic *t*-butyl ethers are prepared by acid-catalyzed condensation of *t*-butyl alcohol with the corresponding alcohol [4], Olson and co-worker [5] tried the same method with phenol and *t*-butanol and different acids as catalysts, but the yields were always less than 10 %. Further, *t*-butyl *p*-tolyl ether was prepared by McKinley [6] in a 7 % yield from *p*-cresoxymagnesium bromide and *t*-butyl chloride. By a systematic study of the acid catalyzed interaction of isobutylene and phenols, according to the method of Evans and Edlund [7], Stevens *et al.* [8, 9] succeeded in preparing *t*-butyl aryl ethers:



A recent method of Beringer [10] consisted of the reaction of diphenyliodonium chloride with potassium *t*-butoxide and gives a mixture of iodobenzene and *t*-butyl phenyl ether according to the following:



A successful Williamson-type synthesis of an aromatic *t*-butyl ether has been performed by Bowden and co-worker [11] and Baddely *et al.* [12] using *p*-fluoronitrobenzene and potassium *t*-butoxide in *t*-butanol.

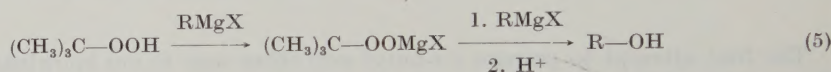


¹ Part XI. Lawesson, S.-O., Busch, T., and Berglund, C., *Acta Chem. Scand.* 15, 260 (1961).

Finally, in a recent publication by Lawesson and Yang [13] it was shown that by reacting *t*-butyl perbenzoate with a Grignard reagent, the oxygen-oxygen bond is split and the *t*-butyl ether is formed in high yields according to the following stoichiometry:

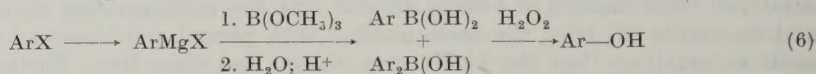


Some elucidation [13] of the mechanism for the oxidation of a Grignard reagent with oxygen was made by reacting a Grignard reagent with *t*-butyl hydroperoxide, in which case the hydroxy compound is the final product.

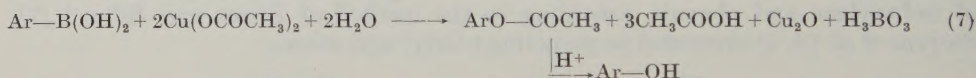


This last method transforms a halide into a hydroxy compound under mild conditions.

In connection with this last method (eqn. (5)), attention is focussed on some other mild methods; in Hawthorne's procedure [14], the overall reaction sequence employed is illustrated in the following formulation:



and Holzbecker's [15] conversion of arylboronic acids to phenols by copper acetate:



see also similar work in the ferrocene series [16].

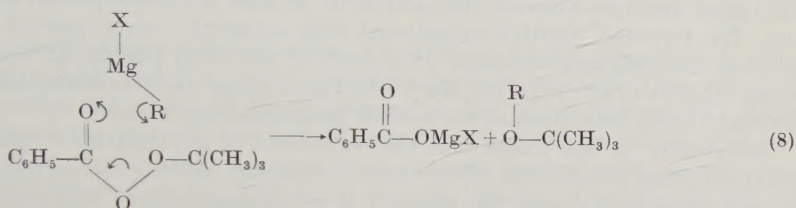
The findings of Smith [1] regarding pyrolysis of *t*-butyl phenyl ether prompted us to reinvestigate his work. We felt also that the reaction of Grignard reagents with *t*-butyl hydroperoxide is of limited practical importance and therefore we have tried to convert aryl halides to the corresponding hydroxy compounds via *t*-butyl ethers.

Lawesson and Yang [13] have earlier prepared four *t*-butyl aryl ethers from Grignard reagents and *t*-butyl perbenzoate in yields varying from 65–81 %. We have synthesized some new *t*-butyl phenyl ethers and found that, if a greater excess of Grignard reagent is used than before, higher yields of products are obtained. High yields of *t*-butyl *m*-tolyl ether, *t*-butyl *o*-tolyl ether, *t*-butyl phenyl ether and *t*-butyl 2-thienyl ether were thus obtained. However, in the case of some *p*-substituted *t*-butyls phenyl ethers, the yields could vary and, following the regular procedure of work-up, there was always a smell of phenol from the acid fraction indicating that some decomposition had occurred. The sensitivity of *t*-butyl *p*-tolyl ether and *t*-butyl *p*-anisyl ether to heat will be discussed in what follows.

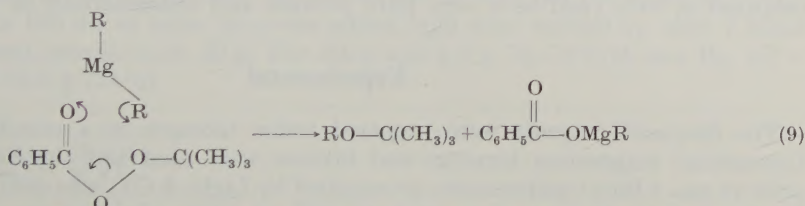
In some experiments, we prepared *t*-butyl phenyl ether and *t*-butyl 2-thienyl ether from Grignard reagents and *t*-butyl peracetate and, based on yields of products, this is a good alternative method. With organo-lithium reagents, it was found that the yields of ether were less than 32 % and that high-boiling products were formed, presumably through a primary attack of the lithium compound on the carbonyl group. As organo-lithium compounds are easily converted to Grignard reagents with

anhydrous MgBr_2 , *t*-butyl ethers might be prepared in this way, and it does not in any way limit the synthetic utilities of the method [17].

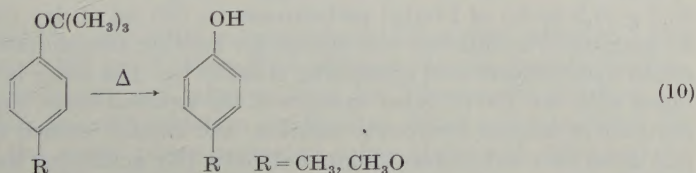
In part I of this series [13], the reaction between Grignard reagents and *t*-butyl perbenzoate was said to be formulated as



These formulas should not be accepted literally, as the symbol RMgX is inadequate to explain the behaviour of the Grignard reagent; RMgX , being convenient to express, is instead employed as a simplification. It is known from work by Dessy *et al.* [18] that Grignard reagents are complex mixtures containing two types of magnesium, magnesium halide and dialkyl- and diarylmagnesium. Since these types of magnesium do not exchange readily, a Grignard reagent is better represented constitutionally as $\text{R}_2\text{Mg} \cdot \text{MgX}_2$, rather than RMgX and the conventional Schlenk equilibrium. We have reacted *t*-butyl perbenzoate with diethylmagnesium and identified ethyl *t*-butyl ether and benzoic acid; on the other hand, *t*-butyl perbenzoate with magnesium bromide in the presence of cyclohexene gave trans-1,2-dibromocyclohexane. The formation of *t*-butyl ethers from Grignard reagents and *t*-butyl perbenzoate might thus also be formulated as follows:



A study of the stability of the prepared ethers revealed that *t*-butyl phenyl ether is a rather stable compound. It was, for instance, possible to distil it at normal pressure without noticeable dealkylation. When refluxed for 23–24 hours at an oil bath temperature of 200°C , no decomposition was observed, *t*-butyl phenyl ether being recovered quantitatively. *t*-Butyl *o*-tolyl ether, *t*-butyl *m*-tolyl ether and *t*-butyl *p*-bromophenyl ether were also found to be as stable to heat as *t*-butyl phenyl ether. Smith's claim [1] that *t*-butyl phenyl ether is sensitive to heat is therefore rejected. However, *t*-butyl *p*-tolyl ether and *t*-butyl *p*-anisyl ether decomposed very fast on heating and gave the corresponding phenols without alkylation of the nucleus

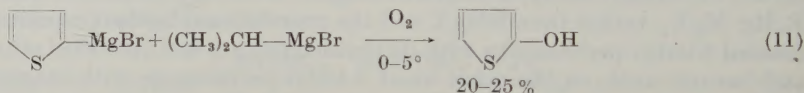


The same ethers redistilled under absolutely neutral conditions gave the same result and these appear to be the first known thermally unstable *t*-butyl aryl ethers.

As indicated, very little work has been published on the dealkylation of *t*-butyl aryl ethers; Smith [1] rearranged *t*-butyl phenyl ether with aluminium chloride, Beringer [10] used titanium tetrachloride and both isolated *p*-*t*-butyl phenol as the sole product. We repeated Smith's experiment with authentic *t*-butyl phenyl ether and aluminium chloride and obtained 71 % yield of *p*-*t*-butyl phenol. It is apparent that, using Friedel-Crafts catalyst, the *t*-butyl aryl ethers are first dealkylated followed by Friedel-Crafts alkylation of the phenol simultaneously formed.

Eventually, it was found that the conversion of aryl halides to phenols could be attained using *p*-toluenesulphonic acid as catalyst; heating the corresponding *t*-butyl phenyl ether with a catalytic amount of *p*-toluenesulphonic acid caused decomposition and generally the phenols were obtained in high yields. In a few cases alkylation occurred to a minor extent, however.

This method, which does not seem to have any precedent, should be very convenient for the preparation of hydroxythiophenes; for example 2-hydroxythiophene has been prepared by Hurd and Kreuz [19] in low yields from 2-thienylmagnesium bromide, which was oxidized in the presence of excess of isopropylmagnesium bromide



and it has recently been shown [20], that 2-hydroxythiophene at room temperature mainly exists as 3-thiolene-2-one. By the present method, 2-hydroxythiophene was prepared in 94 % yield as a very pure product and characterized as the benzoate.

Experimental

The Grignard reagents were prepared under nitrogen in a common assembly. Commercial magnesium turnings and lithium were used and the halides distilled prior to use. *t*-Butyl perbenzoate, as supplied by Light & Co., was used without purification but dried over sodium sulphate. ($n_D^{20} = 1.5000$). *t*-Butyl peracetate, Lupersol $\neq 7$ was supplied by Lucidol Division, Wallace and Tiernan, Inc., Buffalo, N.Y., and used without purification. Infrared curves were recorded on an Infracord. Analyses were made by the Department of Analytical Chemistry, Uppsala University, and by Dr. A. Bernhardt, Mülheim (Ruhr).

Preparation of *t*-butyl ethers

t-Butyl phenyl ether. Phenylmagnesium bromide was prepared from 13 g of magnesium turnings and 79 g of bromobenzene in 200 ml of ether. Another 200 ml of anhydrous ether were added to the Grignard reagent, the flask cooled in an ice-bath and 58.3 g (0.3 mole) of *t*-butyl perbenzoate in 120 ml of dry ether added dropwise for 30 minutes. The mixture was stirred for another five minutes and then poured into dilute hydrochloric acid containing crushed ice. The ether layer was separated, combined with two 150 ml ether extracts of the aqueous layer, extracted with three 25 ml portions of sodium hydroxide solution, and finally washed until neutral with water and dried over anhydrous sodium sulphate. (By acidifying the basic solution, 29-32 g

of benzoic acid were isolated.) After removal of the solvent, the product was distilled under reduced pressure and gave a yield of 36–40 g (80–89 %) of *t*-butyl phenyl ether boiling at 57–59°C/7 mm Hg. $n_D^{20} = 1.4884$. Distillation at normal pressure gave the b.p. 183–184°C. $n_D^{20} = 1.4884$.

t-Butyl phenyl ether from *t*-butyl peracetate. 0.2 moles of *t*-butyl peracetate in benzene was slowly added to 0.3 moles of phenylmagnesium bromide (from 8.5 g of magnesium turnings and 47.1 g of bromobenzene) in 100 ml of ether at 0°C. After stirring for 3 hours the mixture was poured into ice-water + hydrochloric acid, extracted with ether three times, the combined extracts washed until neutral with water, dried and distilled giving 20 g (67 %) of *t*-butyl phenyl ether, b.p. 57–59°C/8 mm Hg. $n_D^{20} = 1.4880$.

t-Butyl *o*-tolyl ether. The Grignard reagent, prepared from 16 g of magnesium and 102.6 g of *o*-tolylbromide in 300 ml of dry ether was cooled in an ice-water bath and 0.4 mole of *t*-butyl perbenzoate in 100 ml of ether added for 45 minutes. The solution was stirred overnight and worked up in the usual way. Isolated benzoic acid = 46 g (smell of phenol). The ether had a b.p. 75–77°C/10 mm Hg. $n_D^{20} = 1.4928$. Yield 52.5 g (80 %).

Anal. $C_{11}H_{16}O$.

Calc. C 80.44 H 9.83

Found C 80.25 H 9.82

t-Butyl *m*-tolyl ether. The Grignard reagent was prepared from 102.6 g (0.6 mole) of *m*-bromotoluene in 200 ml of ether. It was cooled to zero and 0.4 moles of *t*-butyl perbenzoate in 100 ml of ether dropwise added, and then worked up after 2 hours stirring. Isolated benzoic acid: 29 g. The ether had a b.p. 76–78°C/10 mm Hg. $n_D^{20} = 1.4908$. Yield 48.5 g (74 %).

Anal. $C_{11}H_{16}O$.

Calc. C 80.44 H 9.83

Found C 80.47 H 9.74

t-Butyl *p*-bromophenyl ether. The Grignard reagent was prepared from 82.6 g of *p*-dibromobenzene and 9.25 g of magnesium turnings in 350 ml of dry ether and to the cooled solution, 0.2 moles of *t*-butyl perbenzoate in 100 ml of anhydrous ether added dropwise. The solution was stirred overnight and worked up following the usual procedure. (Benzoic acid = 17 g.) Distillation of the neutral fraction gave a free fraction of bromobenzene and the main fraction with b.p. 63–65°C/0.4 mm Hg; $n_D^{20} = 1.5280$. Yield 32.9 g (72 %).

Anal. $C_{10}H_{13}OBr$

Calc. C 52.44 H 5.72

Found C 52.29 H 5.62

p-*t*-Butoxy-benzoic acid 12.8 g of *t*-butyl *p*-bromophenyl ether were added to 1.58 g of magnesium covered with 100 ml of ether. With addition of some crystals of iodine, the reaction started immediately and, after stirring for 2 hours, the solution was poured into dry ice. After the carboxylation was finished, dilute acid was added, the ether phase separated, the water phase extracted a few times with ether and the combined extracts shaken with sodium bicarbonate. The basic layer was extracted

once with ether and then acidified. The white solid was recrystallized from ether and pet. ether. M.p. 140–142°C (Lit. 139–140°C) Yield 5.8 g (53 %).

t-Butyl 2-thienyl ether. The Grignard reagent was prepared from 10 g of magnesium turnings and 48.9 g (0.3 moles) of 2-bromothiophene. To the cooled solution, 45 ml (0.225 moles) of *t*-butyl perbenzoate in 125 ml of ether was added dropwise. While stirring for 3 hours the temperature was allowed to reach room temperature and the work-up as used in the usual manner: 19 g of benzoic acid was isolated. The ether had b.p. 66°C/11 mm Hg. $n_D^{20} = 1.4994$. Yield 30 g (77 %).

Anal $C_8H_{12}OS$

Calc. C 61.52 H 7.75

Found C 60.99 H 7.64

The same ether was also prepared from *t*-butyl peracetate and the yield from one experiment was 67 %.

The reaction of magnesium bromide with t-butyl perbenzoate

Anhydrous magnesium bromide was prepared from 47 g (0.25 moles) of ethylene bromide and 7.3 g (0.3 moles) of magnesium turnings in 250 ml of ether. 75 ml of cyclohexene were added and the reaction mixture cooled to 0°C, after which 40 ml (0.2 moles) of *t*-butyl perbenzoate in 100 ml of ether were added dropwise during 70 minutes. After stirring for 18 hours (the mixture was allowed to warm to room temperature) and following the usual work-up, 20 g of benzoic acid and 27 g (56 %) of 1,2-dibromocyclohexane (b.p. 49–51°C/0.2 mm Hg, $n_D^{20} = 1.5515$) were obtained.

The reaction of diethylmagnesium with t-butyl perbenzoate

From 0.3 moles of ethylmagnesium bromide in 150 ml of ether, magnesium bromide was precipitated as the dioxane-complex. The ether-dioxane solution of diethylmagnesium was added dropwise to *t*-butyl perbenzoate (10 ml) in ether and stirred for 24 hours (refluxed for the last two hours). The mixture was poured into a saturated ammonium chloride solution and extracted with ether. From the ether extracts, 3.2 g benzoic acid were isolated and from the neutral ether extracts, dried over sodium sulphate (peroxide test: pos!), a low boiling fraction was flask-distilled at reduced pressure. Redistillation gave a fraction with the b.p. 60–100°C and ethyl *t*-butyl ether was identified by V.P.C. Fractional distillation was unsuccessful.

Pyrolysis of t-butyl ethers

t-Butyl phenyl ether. 15 g of the ether were refluxed for 24 hours at 200°C. No change was observed and the ether was neutral. 0.1 g of *p*-toluenesulphonic acid (TS) were added and gentle reflux was maintained. There was violent gas evolution. Distillation gave a main fraction with b.p. 74–76°C/10 mm Hg, which solidified: m.p. 39–40° identical with phenol. Yield 6.3 g (67 %). A higher-boiling product, b.p. 110–120°C/10 mm Hg weighed 2.4 g and solidified. M.p. and mixed m.p. with *p*-*t*-butyl phenol, 99–100°C.

t-Butyl *o*-tolyl ether. 16.4 g of the ether were refluxed for 15.5 hours on an oil bath at a temperature of 200°C without any dealkylation. After addition of 0.1 g of TS

a violent gas evolution started. Distillation gave quantitative yields of *o*-cresol with b.p. 75–77°C/10 mm Hg, $n_D^{20} = 1.5402$, in all respects identical with an authentic sample. No higher boiling product was found.

t-Butyl *m*-tolyl ether. 16.4 g of the ether were refluxed on an oil bath at a temperature of 200°C for 11 hours without any dealkylation. When 0.1 g of TS was added, gas evolution started. Distillation gave 7 g of *m*-cresol, b.p. 84–86°C/8 mm Hg, $n_D^{20} = 1.5381$, identified with authentic *m*-cresol by V.P.C. A higher-boiling fraction, b.p. 90–110°C/8 mm Hg, was shown by V.P.C. to be a 1:1 mixture of *p*-cresol and 3-methyl-6-*t*-butyl phenol.

t-Butyl *p*-tolyl ether. 8 g of the ether was heated on an oil bath at a temperature of 200°C. Gas evolution was observed; distillation gave quantitative of *p*-cresol, b.p. 84–86°C/10 mm Hg, $n_D^{20} = 1.5390$, identical with authentic *p*-cresol (V.P.C.)

t-Butyl *p*-anisyl ether. 18 g of the ether were heated at an oil bath temperature of 150°C. There was a change of colour and gas evolution was observed. Distillation gave quantitative yields of a product (*p*-methoxy phenol) with b.p. 119–120°C/12 mm Hg, which solidified (m.p. 52–54°C). No higher-boiling fraction was found.

t-Butyl 2-thienyl ether. 37.2 g (0.24 moles) of the ether and 0.1 g of TS were placed in a distillation set, connected to a water pump. (Nitrogen was drawn through the capillary.) The flask was placed in an oil bath of 170°C and decomposition started immediately. After 3–5 minutes the pressure was constant and an immediate distillation gave 2-hydroxythiophene, b.p. 85–87°C/10 mm Hg, $n_D^{20} = 1.5613$. Yield 22.5 g (94 %). The benzoate, m.p. 44–46°C.

Isomerization of *t*-butyl phenyl ether

13.3 g of aluminium chloride was added with cooling and in portions to 15 g (0.1 mole) of *t*-butyl phenyl ether. After standing for 24 hours dilute hydrochloric acid was added and the water phase was then extracted several times with ether. The combined extracts were shaken with 2 *M* sodium hydroxide solution from which 10.4 g (71 %) of *p*-*t*-butyl phenol was isolated. M.p. and mixed m.p. 98–99°C.

SUMMARY

Some new *t*-butyl phenyl ethers have been prepared by the perbenzoate method and excellent yields of *t*-butyl ethers are obtained if an excess of Grignard reagent is used. *t*-Butyl peracetate also gives ethers with Grignard compounds. Although *t*-butyl *p*-tolyl ether and *t*-butyl *p*-anisyl ether are thermally unstable and are dealkylated without any additive, a series of other phenyl substituted *t*-butyl ethers are stable; when pyrolyzed in the presence of *p*-toluenesulphonic acid, they give the corresponding phenols as main products. The versatility of this dealkylation method is shown when 2-hydroxythiophene is prepared in 94 % yield from *t*-butyl 2-thienyl ether.

ACKNOWLEDGEMENTS

The authors are indebted to the Head of this Institute, Professor A. Fredga, for the facilities put at their disposal and for his interest in this work. Grants from *Statens Naturvetenskapliga Forskningsråd* and *Lucidol Division, Wallace and Tiernan, Inc., Buffalo, N.Y.* are gratefully acknowledged.

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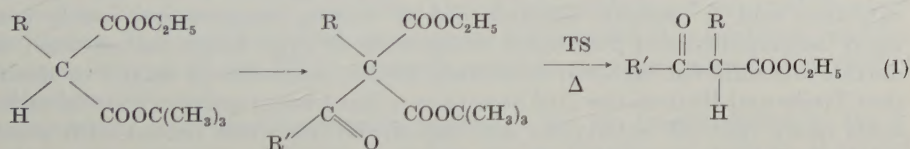
Studies on elimination. I

The formation of olefins by decomposition of β -ketoesters

By CHRISTER FRISELL and SVEN-OLOV LAWESSON

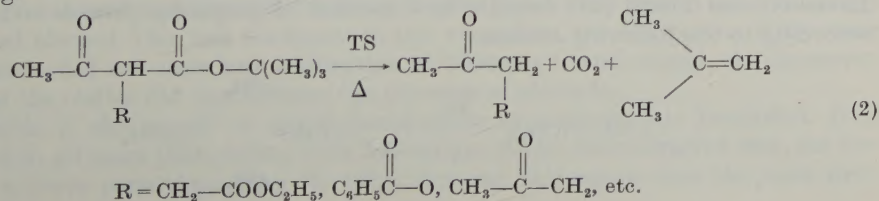
In connection with investigations on copper-salt catalyzed decomposition of peresters in the presence of different substrates [1], it was found desirable to obtain pure 1-methylcyclohexene. It is reported [2-4] that pyrolysis of 1-methylcyclohexylacetate yields about 75 % of 1-methylcyclohexene mixed with 25 % of methylenecyclohexane, and pyrolysis according to Chugaev [5] gives a ratio of 79/21 of the same products. Quite recently, two review articles [6, 7] have been published on elimination reactions. As seen from the sequel, we have for some time been using a method which is a type of 1,2-elimination different from those mentioned in the recent articles [6, 7]. A study of such reactions has been started as it is imagined that a closer and more thorough investigation would be successful and not irrelevant. This paper, which we consider to be of a preliminary character, deals with β -ketoesters derived from three 1-alkylcyclohexanols and one alkylcyclohexylcarbinol.

Hauser and his associates [8] found, as late as 1944, that *t*-butyl hydrogen malonate on heating undergoes an elimination reaction to form isobutylene and malonic acid, in contrast to ethyl hydrogen malonate which undergoes the common decarboxylation reaction. This discovery was further adapted for a new and general method for the preparation of β -ketoesters [9, 10] according to the following flow-diagram:

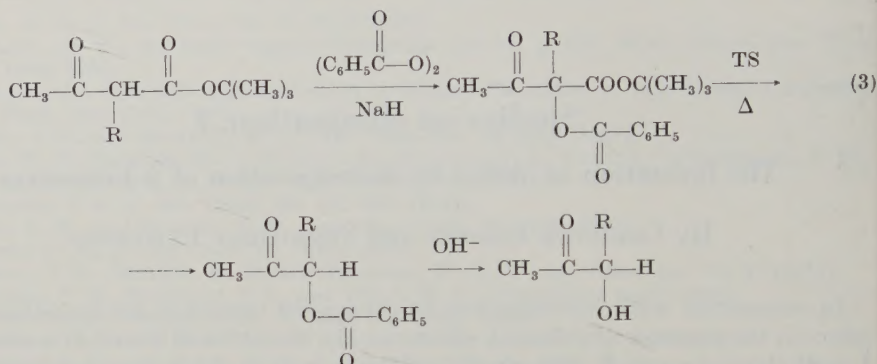


where *TS* = *p*-toluenesulphonic acid.

Inspired by Hauser's findings, new routes to ketones were found. Fonken and Johnson [11] used di-*t*-butyl malonates as starting materials and Renfrow and Walker [12] started from *t*-butyl acetoacetates. Treibs and Hintermeier [13] have, in an inspiring piece of work, made *t*-butyl acetoacetate easily available by reacting *t*-butanol with diketene and thereafter they carried out a series of reactions such as the following:

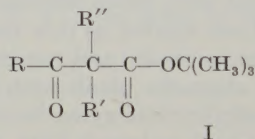


Quite recently Lawesson and Grönwall [14] worked out a new route to acyloins:



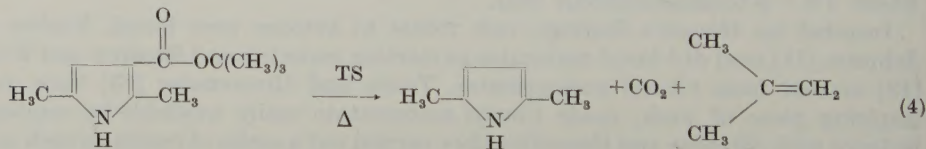
and Lawesson and Dahlén [15] are presently working on compounds of the same type.

A characteristic of all the structures investigated [8-15] is that they are all β -carbonyl compounds of type I,

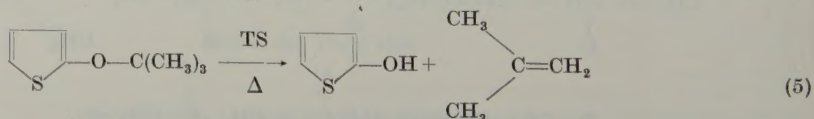


where $R = \text{OC}_2\text{H}_5$, $\text{OC}(\text{CH}_3)_3$, or CH_3 , and R' and R'' are different functional or alkyl groups.

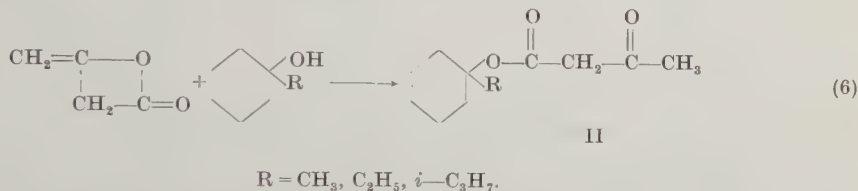
As far as we know, the only compounds investigated are *t*-butyl esters and that the olefin generated, isobutylene, has not been the main goal of the syntheses. *p*-Toluenesulphonic acid in catalytic amounts and at varying temperatures, easily causes a rapid decomposition of β -carbonyl compounds of type I into isobutylene, carbon dioxide and different carbonyl structures. In this connection it should be mentioned that Treibs and Hintermeier [16] have shown that *t*-butyl esters of pyrrole carboxylic acids easily split off isobutylene and carbon dioxide when heated with *p*-toluenesulphonic acid, for example



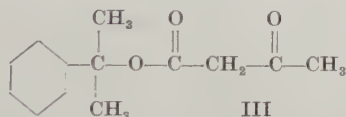
Lawesson and Frisell [17] found a new method of preparing phenols and thienols according to the following scheme:



The preparation of most alkyl acetoacetates is performed by the classical Claisen condensation or ester exchange, but these methods seem to be rather cumbersome with the more complicated alcohols. However, according to Boese [18, 19], a simple and convenient method is to react diketene with alcohols having catalytic amounts of acids present. Pohl and Schmidt [20] used tertiary amines and Treibs and Hintermeier [13] sodium acetate as the catalysts. By adapting the Treibs' procedure we found that diketene reacted smoothly with a series of 1-alkylcyclohexanols at 80–90°C in the presence of small amounts of sodium acetate:



Dimethylcyclohexylcarbinol was found to react with diketene in a similar way, giving III:



In two cases (II: $\text{R} = \text{CH}_3, \text{C}_2\text{H}_5$) it was possible to obtain analytically pure substances. In the other cases, some decomposition occurred during the distillations. With $\text{R} = i\text{-C}_3\text{H}_7$, a high yield of the distilled product was isolated, but from the IR-spectrum it was seen that the sample contained small amounts of a hydroxy derivative (absorption 3400–3350 cm^{-1}), presumably the parent alcohol. Compound III seemed to decompose easily and it was almost impossible to get any crude product by distillation. It is supposed that at increased temperature it is relatively easy for β -ketoesters of types II and III to fragment partly to give the corresponding alcohol and dehydroacetic acid.

In connection with the experimental procedure for the fragmentation of the β -ketoesters, giving mostly a mixture of olefins, carbon dioxide and acetone, it should be said that only II ($\text{R} = \text{CH}_3, \text{C}_2\text{H}_5$) was available as a pure and uniform liquid. When using II ($\text{R} = i\text{-C}_3\text{H}_7$) and III in some experiments, these samples contained the alcohol, from which the corresponding β -ketoester had been prepared and dehydroacetic acid, of course, and a mixture of olefins and alcohol was obtained after fragmentation. In the following decomposition experiments, however, the β -ketoesters (II: $\text{R} = i\text{-C}_3\text{H}_7$; III) were used directly when the reaction between diketene and the corresponding alcohol was complete. Always, an excess of diketene to alcohol was used and thus the crude, undistilled β -ketoester should not contain any unreacted alcohol. This was confirmed in two ways: first, the IR-spectra of the crude β -ketoesters did not show any absorption at 3500 cm^{-1} , and second, the chromatograms of the olefins did not indicate the presence of alcohols.

In Table 1, the results of our decomposition experiments are tabulated. It is observed in all cases that olefins, with a bond *exo* to the six-membered ring, are formed in a lower percentage than the other isomers; this means that the more ther-

Table 1. Decomposition of β -ketoesters: $\text{CH}_3-\overset{\text{O}}{\parallel}\text{C}-\text{CH}_2-\overset{\text{O}}{\parallel}\text{C}-\text{O}-\text{R}$.

R	Yield of olefin (%)	B.p. of olefin mixture ($^{\circ}\text{C}$)	Temp. of decomp. ($^{\circ}\text{C}$)	% exo-isomer ^{a,b}
 CH_3	82	100-112	130	6
 C_2H_5	85	133-136	160	0
 $\text{CH}(\text{CH}_3)_2$	63 ^c	145-155	175	12
 CH_3	61 ^c	154-160	170	40

^a The values listed indicate the percentage of the fragmentation product obtained having the double bond *exo* to the ring. The differences between these values and 100 % would represent the percentage of the total olefin constituting the other possible isomer.

^b These values were obtained by gas chromatography.

^c The β -ketoesters were not isolated.

modynamically stable olefin predominates, and, in two cases, would account for the fact that a primary or secondary hydrogen was removed rather than a tertiary one.

Benkeser *et al.* [5] observed isomerization of certain olefins when refluxed in glacial acetic acid for 24 hours with *p*-toluenesulphonic acid present, although in our cases we observed that the small amount of *p*-toluenesulphonic acid used in the decomposition experiments for up to 2 hours did not cause any isomerization. Analysis by VPC did not show any change of olefin composition when a mixture of 1-methylcyclohexene and methylenecyclohexane was distilled from *p*-toluenesulphonic acid.

Finally, it should be stressed that at this stage of the investigation we do not intend to draw any conclusions regarding mechanistic aspects etc. and further statements await a more complete investigation. However, in regard to the synthetic utility of this method, we may say that the procedures are very simple and rapid, that the yields are good and the products easy to work up. At present the method seems to be limited to esters of tertiary alcohols but work along different lines is in progress to test the versatility of the method.

Experimental

Diketene as supplied by Schuchardt was used after distillation. The alcohols were prepared according to known procedures [21-23]. Elementary analyses were made by the Analytical Department of Uppsala University, as well as the VPC investigations. Boiling points are not corrected.

Preparation of 1-methylcyclohexylacetoacetate

50 g (0.44 mole) of 1-methylcyclohexanol were heated to 80–90°C, after which the oil bath was taken away and 0.25 g of water-free sodium acetate added. 38.5 ml (0.50 mole = 42.0 g) of diketene was then added dropwise to the heated alcohol for 40 minutes. There was an exothermic reaction. The reaction mixture refluxed gently during the addition and was stirred for three hours while the temperature was allowed to decrease to room temperature. Distillation gave a fraction boiling at 78–80°C/0.4 mm Hg. $n_D^{20} = 1.4657$. Yield: 65 g (75 %).

Analysis. $C_{11}H_{18}O_3$ (198.3)

Calc. C 66.64 H 9.15

Found C 66.72 H 9.16

Preparation of 1-ethylcyclohexylacetoacetate

To 33.3 g (0.26 mole) of 1-ethylcyclohexanol, heated to 80–90°C, 23.1 ml (0.30 mole = 25.2 g) of diketene was added for 25 minutes. Before the addition of diketene the oil bath was removed and 0.1 g of water-free sodium acetate added. The reaction was exothermic. The reaction mixture refluxed gently and became dark during the addition of the diketene. After three hours' stirring at room temperature, the reaction product was distilled under reduced pressure. B.p. 75–77°C/0.3 mm Hg. $n_D^{20} = 1.4681$. Yield: 44.9 g (81 %).

Analysis. $C_{12}H_{20}O_3$ (212.3)

Calc. C 67.89 H 9.50

Found C 67.30 H 9.35

Preparation of 1-isopropylcyclohexylacetoacetate

After heating 37 g (0.26 mole) of 1-isopropylcyclohexanol to 80–90°C and taking away the oil bath, 0.1 g of water-free sodium acetate was added and then, dropwise, 24 ml (0.31 mole = 26.1 g) of diketene. The reaction mixture refluxed gently and because of the exothermic reaction became dark. The diketene was added over 25 minutes and, after stirring for 1.5 hours, the product was distilled. B.p. 90–92°C/0.4 mm Hg. $n_D^{20} = 1.4627$. Yield: 47.1 g (80 %). Satisfactory analyses were not obtained as the ester was contaminated with 1-isopropylcyclohexanol.

Preparation of dimethylcyclohexylcarbinylacetoacetate

40 g (0.28 mole) of dimethylcyclohexylcarbinol were heated to 80–90°C for 10 minutes, the oil bath taken away and 0.20 g of water-free sodium acetate added. For 20 minutes, 25.5 ml (0.33 mole = 27.8 g) of diketene was added dropwise. The reaction mixture became dark and refluxed gently as the reaction was exothermic. After stirring for 1.5 hours the product was distilled. B.p. 106–108°C/0.6 mm Hg. $n_D^{20} = 1.4710$. Yield: 46 g (69 %). Satisfactory analyses were not obtained.

Preparation and immediate decomposition of 1-methylcyclohexylacetoacetate

30 g (0.26 mole) of 1-methylcyclohexanol were heated to 80°C. The oil bath was taken away, 0.1 g of water-free sodium acetate added and then dropwise for 25 minutes, 21.6 ml (0.28 mole = 23.5 g) of diketene. After two hours' stirring, 0.05 g of

p-toluenesulphonic acid was added and the mixture placed on an oil bath at 155°C. After two hours' pyrolysis 33 g crude product were obtained. Redistillation gave a low-boiling fraction consisting of acetone and a high-boiling fraction which was a mixture of 1-methylcyclohexene and methylenecyclohexane. B.p. 95–115°C. Yield: 17 g (68 %).

Decomposition of 1-methylcyclohexylacetoacetate

25 g (0.13 mole) of 1-methylcyclohexylacetoacetate were placed with 0.1 g of *p*-toluenesulphonic acid in a distillation apparatus on an oil bath at 130°C. Gas evolution soon began and a liquid distilling. The temperature of the oil bath was gradually raised to 180°C and the temperature of the distillate rose to 100°C. After two hours' pyrolysis, redistillation of the products gave a low-boiling fraction between 58 and 65°C. This consisted mostly of acetone. The high-boiling fraction had the b.p. 100–112°C. This last fraction, a mixture of 1-methylcyclohexene and methylenecyclohexane, weighed 10.2 g. Yield: 82 %.

Preparation and immediate decomposition of 1-ethylcyclohexylacetoacetate

To 33.3 g (0.26 mole) of 1-ethylcyclohexanol heated to 80–90°C, 0.1 g of water-free sodium acetate was added. The oil bath was removed and 23.1 ml (0.30 mole = 25.2 g) of diketene added dropwise for 20 minutes. After 15 minutes 0.1 g of *p*-toluenesulphonic acid was added and the flask containing the reaction mixture placed on an oil bath at 150–160°C. The decomposition began almost immediately and after one hour the pyrolysis was complete. Redistillation of the products gave a low-boiling fraction, consisting of acetone, and a high-boiling fraction, consisting of 1-ethylcyclohexene, having the b.p. 135–138°C. $n_D^{20} = 1.4560$. Yield: 21 g (73 %).

Decomposition of 1-ethylcyclohexylacetoacetate

32 g (0.15 mole) of 1-ethylcyclohexylacetoacetate and 0.1 g of *p*-toluenesulphonic acid were placed in a distillation apparatus on an oil bath at 160°C. The decomposition began immediately and a colourless liquid began to distil. The temperature of the oil bath was gradually raised to 205°C and the highest temperature of the distillate was 136°C. After 2 hours the pyrolysis appeared to be complete and the decomposition products were redistilled. The first fraction consisted of acetone. The other, boiling at 133–136°C, consisted of 1-ethylcyclohexene. $n_D^{20} = 1.4569$. Yield: 14 g (85 %).

Preparation and immediate decomposition of 1-isopropylcyclohexylacetoacetate

After heating 34.1 g (0.24 mole) of 1-isopropylcyclohexanol to 80–90°C and taking away the oil bath, 0.1 g of water-free sodium acetate was added and then, dropwise for 20 minutes, 22.4 ml (0.29 mole = 24.4 g) of diketene. After stirring for 1.5 hours, 0.1 g of *p*-toluenesulphonic acid was added and the mixture placed on an oil bath at 175°C. The decomposition began immediately and a colourless liquid distilled. The temperature of the oil bath was gradually raised to 200°C and the pyrolysis seemed

to be complete after about 2 hours. Redistillation of the reaction products gave acetone and a high-boiling fraction consisting of 1-isopropylcyclohexene and isopropylidenecyclohexane. B.p. 145–155°C. Yield: 19.2 g (63 %).

Preparation and immediate decomposition of dimethylcyclohexylcarbinylacetoacetate

24 g (0.17 mole) of dimethylcyclohexylcarbinol were heated to 80–90°C, the oil bath taken away and 0.1 g of water-free sodium acetate added. For 20 minutes, 16.9 ml (0.22 mole = 18.5 g) of diketene were added dropwise. After stirring for 1.5 hours 0.1 g of *p*-toluenesulphonic acid was added and the flask placed on an oil bath at 170°C. There was immediate decomposition and a colourless liquid distilled. The temperature of the oil bath was gradually raised to 190°C. After 35 minutes' pyrolysis, the decomposition products were redistilled. The first fraction consisted of acetone and the other of 2-cyclohexylpropylene and isopropylidenecyclohexane. B.p. 154–160°C. Yield: 13 g (61 %).

SUMMARY

Acetoacetates have been prepared by reacting diketene with three 1-alkylcyclohexanols and an alkylcyclohexylcarbinol in the presence of catalytic amounts of sodium acetate. Decomposition of the β -ketoesters in the presence of *p*-toluenesulphonic acid and at the temperatures mentioned in Table 1 gives carbon dioxide, acetone and a mixture of olefins, which was analysed by gas chromatography. In two cases, a primary and a secondary hydrogen was removed rather than a tertiary one, so that the thermodynamically more stable olefins are formed.

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We are indebted to the head of this Institute, Prof. A. Fredga, for the facilities put at our disposal and to *Magnus Bergvall's stiftelse* for a grant. Prof. R. A. Benkeser of Purdue University is sincerely thanked for supplying the required olefins for VPC analysis and without whose help this preliminary investigation would have been greatly extended.

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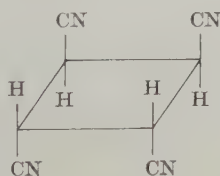
Studies on peroxy compounds

XIII.¹ The introduction of the benzoyloxy group into cyanoacetates

By SVEN-OLOV LAWESSON and CHRISTER FRISELL

Lawesson, Busch and Berglund have shown in earlier communications of this series [1-3] that when the sodium compound of diethyl malonate (in benzene) is reacted with *t*-butyl peracetate, the diethyl *O*-*t*-butyl tartronate is formed in low yields, but when benzoyl peroxide is used, the corresponding *O*-benzoyl tartronate is obtained smoothly and in high yields. As part of a project outlined earlier by us [1], we describe here the reaction between benzoyl peroxide and sodium compounds of cyanoacetate derivatives, and also some unsuccessful experiments with malononitrile.

Acyloxy derivatives of ethyl cyanoacetate have not been prepared earlier. The first known attempt to synthesize ethyl acetoxy cyanoacetate was made quite recently by Sadeh and Berger [4] by treating ethyl bromocyanoacetate with potassium acetate in alcoholic solution, a method similar to that of Conrad and Brückner [5] for the preparation of tartronates. A substance with m.p. 201°C was obtained which, by X-ray, IR, and NMR-studies, was shown to be 1,2,3,4-tetracyanocyclobutane (I) with the following steric formula:



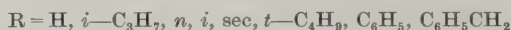
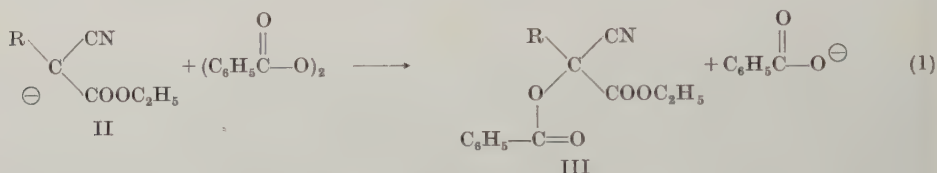
Additional, but unsuccessful experiments were made by Sadeh [4], who changed the conditions in such a way that acetic acid and triethylamine [6] in benzene were used instead of potassium acetate in alcoholic solution. No acetoxy compound was isolated, but 1,2,3-tricarbethoxy cyclopropane [7, 8] was identified in fair yields as the sole product.

Sadeh [9] has recently tried the method of Dimroth and Schweizer [10] for the

¹ Part XII. Lawesson, S.-O., and Frisell, C., Arkiv Kemi 17, 393 (1961).

preparation of diethyl 0-acetyl tartronate from diethyl malonate and lead tetraacetate, but without success. Performing the reaction between ethyl cyanoacetate and lead tetraacetate in different solvents such as chloroform, benzene or glacial acetic acid, the desired product was not obtained but only tars and polymeric material in each case. Sadeh, who needed ethyl acyloxy cyanoacetate for work with amino acid precursors, had thus to postpone further research as this starting material was not available.

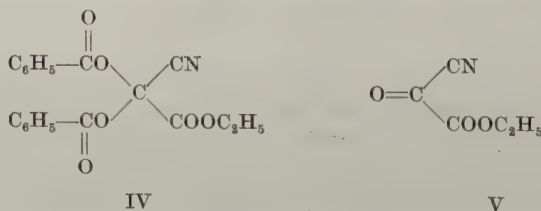
It has now been found that benzoyl peroxide reacts with sodium compounds of ethyl cyanoacetate to give the corresponding benzoyloxy compound. The principle of the method is to prepare the sodium compound from sodium hydride in benzene and the corresponding cyanoacetate, and then add benzoyl peroxide dissolved in benzene to the cooled solution. After stirring overnight or longer, the formed benzoic acid is extracted and the new product purified. Sufficient data have been collected to show that the reaction may be generalized and expressed according to following stoichiometric formula:



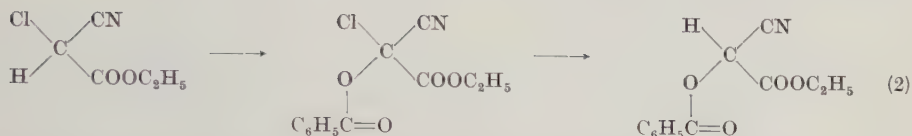
The liquid benzoyloxy compounds are all viscous and seem to be stable for at least one year, and they showed no tendency to decompose on distillation.

When $\text{R} \neq \text{H}$ (eq. (1)) the reaction runs smoothly and quite normal meaning that no gas evolution is observed. However, it was generally found that not all the benzoyl peroxide is consumed, irrespective of an excess of the sodium compound. Also, particularly with alkyl-substituted cyanoacetates, the yields are smaller than with other so-called active methylene compounds. These findings are in contrast to those for malonates and β -ketoesters, for instance, in which cases generally all the benzoyl peroxide is consumed and high yields obtained.

With ethyl cyanoacetate certain complications arose at first; using a small excess of sodium cyanoacetate (II, $\text{R} = \text{H}$) to benzoyl peroxide, only small yields of a solid with a m.p. 127.5–129.5°C were isolated. Gas evolution occurred and the estimated yield of benzoic acid was not isolated. Elementary analysis and mol. wt. determination showed that the compound was the dibenzoyloxyethylated cyanoacetate (IV),



which should be of interest as a derivative of the little-known cyanooxalic ester, V. An attempt to prepare ethyl benzoyloxy cyanoacetate according to the following scheme:

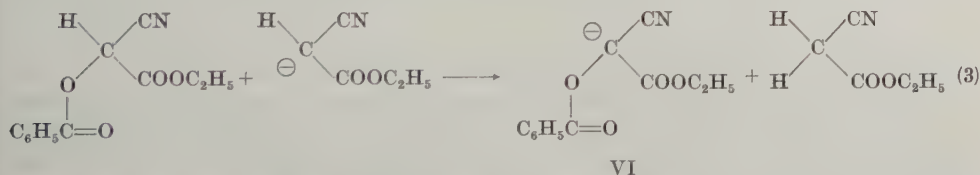


was prevented, as we were unable to prepare ethyl chlorocyanoacetate as described in the literature [11].

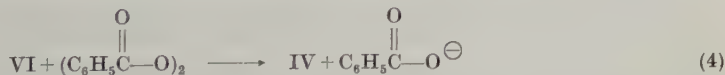
Eventually, it was found that it was of great importance to use absolutely pure starting materials. If 2-3 times redistilled ethyl cyanoacetate and twice recrystallized benzoyl peroxide were used, no gas was evolved, quantitative yields of benzoic acid was isolated and both mono- and disubstituted cyanoacetates were found. By using a large excess of ethyl cyanoacetate to sodium hydride and benzoyl peroxide, we were able to prepare ethyl benzoyloxy cyanoacetate in 60 % yield.

The gas generated during the reaction between sodium cyanoacetate (from the stock) and benzoyl peroxide indicates that the peroxy compound undergoes an induced decomposition. The rupture of the oxygen-oxygen bond of benzoyl peroxide is known to give benzoyloxy radicals [12], which then give phenyl radicals and carbon dioxide. No diphenyl or other by-products were found, although even the careful examinations of the reaction products may have failed to detect small quantities of such products.

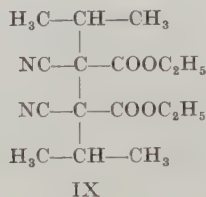
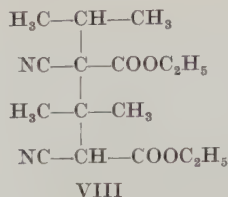
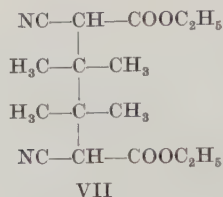
To account for the disubstitution observed when sodium cyanoacetate and benzoyl peroxide react under the usual conditions and in about 1:1 mole ratio, it is assumed that the mono-benzoyloxy compound (III, R=H) first formed, is more acidic than the starting material, and the corresponding sodium compound VI is then immediately formed, according to the following stoichiometry:



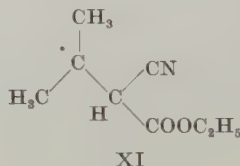
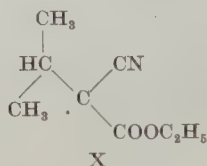
VI then gives the dibenzoyloxy compound IV with benzoyl peroxide.



As no gas is evolved in any of these reactions, we are not inclined to propose a free-radical mechanism but prefer one of the ionic type; the stoichiometry is shown in eq. (1) and eqs. (3) and (4). However, to test this statement further we have generated radicals in a benzene solution of ethyl iso-propyl cyanoacetate by decomposing *t*-butyl perbenzoate with help of catalytic amounts of cuprous chloride. The *t*-butoxy and benzoyloxy radicals thus formed would then be free to react in different ways. We found no benzoate nor any *t*-butoxy derivative and only small amounts of a high-boiling fraction which elementary analysis showed to be the dimer. Alternative structures are possible (VII-IX):

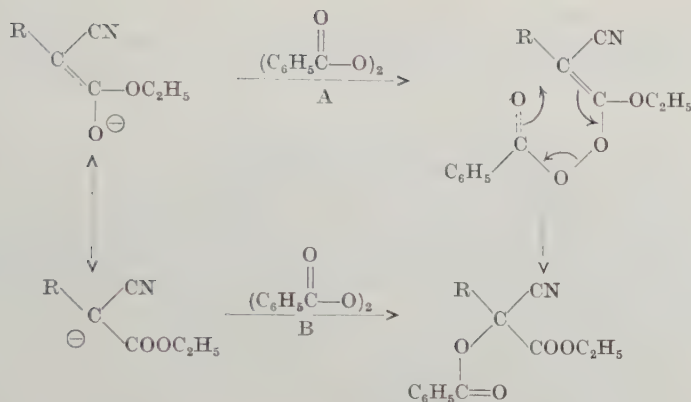


Judging from NMR-analysis, structure VII is excluded; either VIII or IX, or a mixture of both, are plausible structures. This means that a *t*-butoxy or a benzoyloxy radical attacks ethyl iso-propyl cyanoacetate in two ways, giving either of the two radicals X and XI, or both



As VII does not seem to be formed, it is thought that the radical XI is only generated in small amounts compared to X, and that X is the mainly formed radical which dimerizes to IX or also gives an unsymmetrical dimer VIII with XI. Further, it is clear from this experiment that cuprous chloride does not stabilize the intermediate radical X or XI for long enough to allow the benzoyloxy group to be introduced into the cyanoacetate.

Attempts have also been made to prepare IX by treating the sodium compound of ethyl *i*-propyl cyanoacetate with iodide but no dimerization was observed and only ill-defined products containing iodide were found. Finally, it should be said that, although it was early realized that the resemblance might be only formal between the reaction of benzoyl peroxide with sodium compounds of cyanoacetates and cuprous chloride catalyzed decomposition of *t*-butyl perbenzoate in the presence of cyanoacetates, there are strong indications that the named reactions are of an ionic type and that a conventional free-radical mechanism must be rejected. Further, as nucleophiles such as phenols [13], phosphines [14] and amines [15] attack benzoyl peroxide at the oxygen-oxygen bond, it should not be too irrelevant to assume a similar mechanism for the reaction between sodium cyanoacetate and benzoyl peroxide. In this case, the enolate may give an unstable perester as transition state which then rearranges to the benzoyloxy compound (Scheme I, route A),

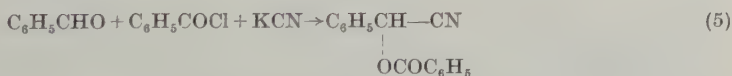


Scheme 1

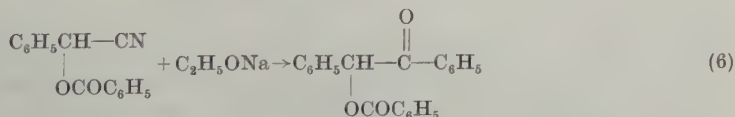
or the carbanion may give the benzoyloxy compound directly (Scheme 1, Route B). Further experiments with benzoyl peroxide (carbonyl O^{18}) are being made before conclusions will be drawn.

Having a series of ethyl benzoyloxy cyanoacetates available, we attempted to find out (in a few cases) what would happen on ethanolysis. Thus, when ethyl phenyl benzoyloxy cyanoacetate was treated with sodium ethoxide in ethanol, we were able to isolate ethyl benzoate, mandelic acid and benzoin as the only products. In a series of carefully performed experiments under different conditions, we tried unsuccessfully to find other fragmentary products in the reaction mixture; if formed they were in extremely small amounts.

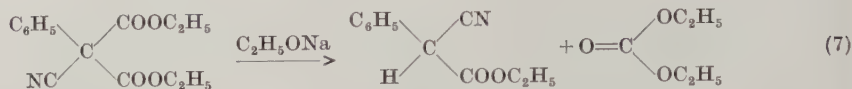
It is rather difficult to explain the formation of some of the isolated products. It is known, however, that benzoyl mandelonitrile is easily obtained by shaking benzaldehyde, potassium cyanide solution and benzoyl chloride under controlled temperature [16, 17].



Sodium alkoxide then gives O-benzoylbenzoin [18, 19] as follows



and further, the yield increases if an aldehyde is added before the treatment with base. This work is claimed to be a confirmation of Lapworth's hypothesis [20, 21] that the first stage of the benzoin condensation is the formation of mandelonitrile which then condenses with the free aldehyde. We have also shown that, when diethyl phenyl cyanomalonate is treated with sodium ethoxide, diethyl carbonate and ethyl phenyl cyanoacetate is formed according to the following:



The point at which the ethoxide ion first attacks III ($\text{R} = \text{C}_6\text{H}_5$) is difficult to determine. Although we could not isolate any diethyl carbonate, the small amounts of benzoin found could have been generated by elimination of the carbethoxy group, in which case, benzoyl mandelonitrile is formed. The *O*-benzoylbenzoin is then formed according to eq. (6) and in the presence of sodium ethoxide, transesterification gives the free benzoin. However, we believe that the main attack is on the benzoyl group resulting in the formation of ethyl benzoate and the cyanohydrin of ethyl benzoylformate, the fate of which is unknown in details. Based on the final products, we postulate, that the cyanohydrin decomposes to ethyl benzoylformate which is converted to ethyl benzoate by the alcoholate.

Ethanolysis of other benzoyloxy derivatives of cyanoacetate gave ethyl benzoate and other products mostly ill-defined.

Malononitrile did not react with sodium hydride in benzene. Apparently the hydride was inactivated and/or covered with the first formed sodium compound of malononitrile. Using an "entrainer" technique [22], only the malononitrile dimer [23] was isolated. Benzyl malononitrile, which is possible to prepare by alkylation, led to no well-defined products.

Experimental

All reactions between sodium cyanoacetate and benzoyl peroxide were performed in a common assembly and in a dry atmosphere. Commercial (Kebo) benzoyl peroxide was used in all experiments, after recrystallization from chloroform and methanol at low temperature. *t*-Butyl perbenzoate ($n_D^{20} = 1.5000$), purchased from Light & Co, was used without further purification. The infra-red spectra measurements were made on a Perkin-Elmer Model 21, double-beam spectrophotometer and an Infracord. The analysis were made by Dr. A. Bernhardt, Mülheim (Ruhr) and by the Analytical Department, Uppsala University. Boiling and melting points are uncorrected. The gases generated during the reaction were collected over saturated, aqueous solution of sodium chloride, saturated with carbon dioxide.

Starting material

By alkylation of ethyl cyanoacetate the following compounds were obtained: ethyl *i*-propyl cyanoacetate [24], b.p. 53–55°C/0.5 mm Hg, $n_D^{20} = 1.4250$; ethyl *n*-butyl cyanoacetate [25], b.p. 74–76°C/0.6 mm Hg, $n_D^{20} = 1.4288$; ethyl *i*-butyl cyanoacetate [25], b.p. 59–60°C/0.2 mm Hg, $n_D^{20} = 1.4300$; ethyl *sec*-butyl cyanoacetate [26], b.p. 60–62°C/0.2 mm Hg, $n_D^{20} = 1.4296$; and ethyl benzyl cyanoacetate [27], b.p. 116–119°C/0.6 mm Hg, $n_D^{20} = 1.5027$. Ethyl phenyl cyanoacetate was prepared according to Widequist [28] from benzyl cyanide and diethyl chloroformate, b.p. 95–97°C/0.2 mm Hg, $n_D^{20} = 1.5055$; diethyl phenyl cyanomalonate [29] from diethyl phenyl cyanoacetate and ethyl chloroformate, b.p. 113–115°C/0.1 mm Hg, $n_D^{20} = 1.4940$. Ethyl 2-cyano-3-ethyl-3-methylhexanoate was prepared according to Bränd-

ström and Forsblad [30], b.p. 125–127°C/10 mm Hg, $n_D^{20} = 1.4446$ (Anal: calc. C 68.21, H 10.02; found C 68.18, H 10.08) and ethyl *t*-butyl cyanoacetate [31] from ethyl isopropylidene cyanoacetate and methylmagnesium iodide b.p. 55–57°C/0.5 mm Hg, $n_D^{20} = 1.4330$.

Ethyl benzoyloxy cyanoacetate

3.6 g (0.15 mol) of sodium hydride were covered with 40 ml of benzene and 56.6 g (0.50 mol) of redistilled ethyl cyanoacetate were added dropwise. After 2 hours all the sodium hydride had been consumed and the sodium compound had precipitated as a white mass. The mixture was cooled to 0°C and 24.2 g (0.1 mol) of benzoyl peroxide in 250 ml of benzene were added in two portions with an interval of 10 minutes. The reaction mixture soon turned yellow and, after 17 hours, the peroxide test was negative. The reaction mixture was poured onto water, the two layers separated, the water phase twice extracted with ether, and then acidified. A quantitative yield of benzoic acid was isolated (12 g). The benzene-ether phases were combined, washed until neutral with water and dried over sodium sulphate. After concentration, distillation gave a colourless, viscous liquid as the main fraction: b.p. 113–115°C/0.2 mm Hg, $n_D^{20} = 1.5058$. Yield: 14 g (60 %). (Calc: C 61.79, H 4.75; found: C 61.79; H 4.98.) When the sodium cyanoacetate was prepared from 0.3 mol of sodium hydride and 0.3 mol of redistilled ethyl cyanoacetate in 300 ml of benzene, and then 0.2 mol of benzoyl peroxide in 300 ml of benzene allowed to react in the usual way, 19 g (41 %) of ethyl benzoyloxy cyanoacetate, b.p. 115°C/0.2 mm Hg, $n_D^{20} = 1.5058$ and 5 g of ethyl dibenzoyloxy cyanoacetate, m.p. 127–129°C (from benzene and pet. ether) (calc: C 64.58, H 4.28, N 3.86; found: C 64.41, H 4.01, N 3.96) were found. If 26.0 g (0.23 mol) of ethyl cyanoacetate (from stock), 5.7 g (0.24 mol) of sodium hydride, and 48.4 g (0.2 mol) of benzoyl peroxide, were allowed to react as above, 4–4.5 l of gas were generated. 15–20 g of benzoic acid were found and only 9 g (13 %) of ethyl dibenzoyloxy cyanoacetate isolated; no monosubstituted product was found.

Ethyl iso-propyl benzoyloxy cyanoacetate

The sodium compound of ethyl iso-propyl cyanoacetate was prepared by a slow addition of 52.6 g (0.34 mol) of ester to 8.05 g of sodium hydride covered with 620 ml of dry benzene. The reaction was run for 22 hours by which time all hydride had been consumed and the solution was almost clear. The solution was cooled in an ice-water bath and 75 g (0.31 mol) of benzoyl peroxide in 775 ml of dry benzene was added for 30 minutes. After 24 hours, the reaction mixture was worked up in the usual way, although the peroxide test was positive. Isolated benzoic acid 31.6 g. The organic phase, dried over sodium sulphate, was concentrated and the final distillation gave a viscous, almost colourless oil as the main fraction, b.p. 133–135°C/0.3 mm Hg, $n_D^{20} = 1.4965$. Yield: 53 g (62 %). (Calc: C 65.44, H 6.22; found: C 65.37, H 6.26.)

Ethyl n-butyl benzoyloxy cyanoacetate

To 2.55 g (0.11 mol) of sodium hydride, covered with 200 ml of dry benzene, 18.0 g (0.11 mol) of ethyl *n*-butyl cyanoacetate were added. The solution soon became turbid as the sodium compound was not soluble in benzene. After 6 hours, the mixture was

cooled in an ice-water bath and 24.2 g (0.1 mol) of benzoyl peroxide in 250 ml of benzene were added dropwise for 15 min. After stirring for 17 hours, the reaction was worked up in the usual way in spite of a positive peroxide test. A quantitative yield of benzoic acid (12.1 g) was isolated. Distillation gave a viscous, almost colourless liquid as the main fraction, b.p. 143–145°C/0.3 mm Hg, $n_D^{20} = 1.4942$. Yield: 10 g (35 %). (Calc: C 66.43, H 6.62; found: C 66.55, H 6.92.)

Ethyl iso-butyl benzoyloxy cyanoacetate

The corresponding sodium salt was prepared by adding 18.0 g (0.11 mol) of ethyl iso-butyl cyanoacetate to 2.55 g (0.11 mol) of sodium hydride in 250 ml of dry benzene. Heat was applied to start the reaction and it was found that the sodium compound was soluble in benzene. After 7 hours, the solution was cooled and benzoyl peroxide (0.1 mol) in 250 ml of benzene was added. Stirring was continued for 16 hours and the solution was then worked up although the peroxide test was positive. 12 g of benzoic acid were obtained. Distillation of the concentrated and dried, ether-benzene phase gave a viscous, faintly yellow liquid: b.p. 146–148°C/0.5 mm Hg, $n_D^{20} = 1.4960$. Yield: 7.5 g (26 %). (Calc: C 66.43, H 6.62; found: C 66.55, H 6.76.)

Ethyl sec-butyl benzoyloxy cyanoacetate

18 g (0.11 mol) of ethyl sec-butyl cyanoacetate were added to an equivalent amount of sodium hydride (2.55 g) in 200 ml of dry benzene. Heat was applied to start the reaction; the formed sodium compound was soluble in benzene. After 2 hours, all hydride had been consumed and 24.2 g (0.1 mol) benzoyl peroxide in 250 ml of benzene were added to the cooled solution. After 20 hours stirring, during which time the temperature of the reaction became equal to room temperature, the peroxide test was positive, but nevertheless the work-up was started. Isolated benzoic acid: 11.1 g. Distillation of the concentrated acid-free solution gave the main fraction with b.p. 150–155°C/0.4 mm Hg. After standing for some time it crystallized; and recrystallization from pet-ether gave white crystals, m.p. 42–44°C. Yield: 15.1 g (52 %). (Calc: C 66.43, H 6.62; found: C 66.94, H 6.54.)

Ethyl t-butyl benzoyloxy cyanoacetate

The sodium compound of ethyl t-butyl cyanoacetate was prepared by adding 20.4 g (0.12 mol) of the ester to 2.9 g (0.12 mol) of sodium hydride covered with 250 ml of dry benzene. The sodium compound was soluble in benzene and after 6 hours, the clear solution was cooled to 0°–5°C and 26.2 g (0.11 mol) of benzoyl peroxide, dissolved in 265 ml of benzene, added in portions for $\frac{1}{2}$ hour. Stirring was continued for 18 hours. The amount of benzoic acid isolated was 10.8 g. After the peroxides in the benzene-water phase had been destroyed, the dried solution was concentrated and the final distillation gave the main fraction as a faintly yellow liquid: b.p. 140–142°C/0.5 mm Hg, $n_D^{20} = 1.4980$. Yield: 13.4 g (42 %). (Calc: C 66.43, H 6.62; found: C 66.32, H 6.49.)

Ethyl phenyl benzoyloxy cyanoacetate

The corresponding sodium compound was obtained as an insoluble, white precipitate by adding 41 g (0.22 mol) of ethyl phenyl cyanoacetate to 5.2 g (0.22 mol) of sodium hydride covered with 400 ml of benzene. After stirring for 7 hours, the

mixture was cooled to 0°C and 48.4 g (0.2 mol) of benzoyl peroxide in 500 ml of dry benzene were added for 30 min. After 17 hours, the peroxide test was still positive but the reaction mixture was still worked up; 21.5 g benzoic acid were isolated. Distillation gave a viscous, yellow liquid: b.p. 184–186°C/0.4 mm Hg, $n_D^{20} = 1.5451$. Yield: 47 g (76 %). (Calc: C 69.90, H 4.89; found: C 70.09, H 4.81.)

Ethyl benzyl benzoyloxy cyanoacetate

To 2.75 g (0.11 mol) sodium hydride, covered with 200 ml of dry benzene, 22.5 g (0.11 mol) of the ester were added dropwise. The benzenesoluble sodium compound was rapidly formed and, after 1 hour, the solution was cooled to 0°C and 24.2 g (0.1 mol) of benzoyl peroxide in 250 ml of dry benzene was added and the mixture stirred at room temperature for 20 hours. The reaction was then worked up: 11.7 g of benzoic acid were isolated, the remaining peroxides were destroyed and, after removing benzene + ether, a solid cake remained; recrystallization from acetone gave colourless crystals, m.p. 85–87°C. Yield: 23.5 g (73 %). (Calc: C 70.57; H 5.30; found C 70.61; H 5.34.)

Ethyl 2-cyano-2-benzoyloxy-3-methyl-3-ethyl hexanoate

The desired sodium compound was prepared from 21.1 g (0.1 mol) of ethyl 2-cyano-3-methyl-3-ethylhexanoate and 2.4 g (0.1 mol) of sodium hydride in 200 ml of dry benzene. The reaction was slow and was sometimes heated to drive the reaction to completion. After 23 hours, the mixture was cooled to 0–5°C and 21 g (0.09 mol) of benzoyl peroxide in 215 ml of benzene were added. After stirring for 24 hours the reaction mixture was worked up, although the peroxide test was positive. The isolated amount of benzoic acid was 7.2 g. Distillation of the product gave a yellow, very viscous oil: b.p. 162–164°C/0.4 mm Hg., $n_D^{20} = 1.5031$. Yield: 7 g (23.5 %), (Calc: 68.68, H 7.60, found: C 68.95, H 7.51.)

Cuprous chloride catalyzed decomposition of t-butyl perbenzoate in ethyl iso-propyl cyanoacetate

A 1000 ml three-necked flask was carefully cleaned and fitted with a stirrer, a dropping funnel and reflux condenser, the top of which was connected to a gas collector. 300 ml of anhydrous benzene, 0.1 g of cuprous chloride and 61.2 g (0.4 mole) of ethyl isopropyl cyanoacetate were placed in the flask. The system was swept with nitrogen gas and the flask maintained at an oil bath temperature of 120°C. 40 ml (0.2 mol) of *t*-butyl perbenzoate in 50 ml of benzene were added dropwise for 60 minutes. A blue colour appeared rapidly and the reaction progress was followed by titration [32]. After 6 hours, the reaction was complete and 1.1 l of gas had been collected. When the solution had reached room temperature, it was shaken 2–3 times with 2 *M* sodium hydroxide solution from which 15.2 g of benzoic acid were precipitated. The benzene-phase was shaken until neutral with water and dried over sodium sulphate. Distillation gave ethyl iso-propyl cyanoacetate (20–25 g) and a fraction with b.p. 139–141°C/0.1 mm Hg, $n_D^{20} = 1.4720$. Yield: 8.5 g. The product was a yellow, viscous liquid which was shown to have double the molecular weight of the starting material. (Calc. for $C_{16}H_{24}O_4N_2$ (308.38): C 62.31; H 7.85; found: C 62.36; H 7.74; $M = 301$.)

The ethanolysis of ethyl phenyl benzoyloxy cyanoacetate

To the alcoholate, prepared from 3.45 g (0.15 mol) of sodium and 100 ml of absolute ethanol, 30.9 g (0.1 mol) of ethyl phenyl benzoyloxy cyanoacetate in 100 ml of ethanol were added dropwise. An exothermic reaction started and the solution soon became red. After stirring for 21 hours at room temperature, the mixture was poured into water. The basic water-phase was shaken 4–5 times with ether; the ether layers were combined, washed until neutral with water, dried over sodium sulphate, and concentrated and distilled: 8.5 g of ethyl benzoate, b.p. 85–87°C/10 mm Hg, $n_D^{20} = 1.5070$ was found and also a solid (4 g) with m.p. 132–134°C (Analysis: C 78.96; H 5.83); the solid was shown to be benzoin, the infrared spectra were superimposable and the mixed m.p. with authentic benzoin not depressed. The water-phase was acidified and extracted with ether in a continuous extraction apparatus. From the ether extracts 6 g of mandelic acid were obtained of which the melting point and mixed melting point with authentic mandelic acid were 116–118°C.

The ethanolysis of diethyl phenyl cyanomalonate

Sodium alcoholate was prepared from 4.6 g of sodium and 150 ml of ethanol; 35.5 g (0.14 mol) of diethyl phenyl cyanomalonate in 100 ml of ethanol were added and, after the exothermic reaction had ceased, the stirring was continued for 21 hours at room temperature. The mixture was poured into water, the basic phase shaken 3–5 times with ether, and after being shaken until neutral with water, was dried over sodium sulphate and distilled. The only product was diethyl carbonate (3 g) with b.p. 126°C/760 mm Hg, $n_D^{20} = 1.3861$. The water-phase was acidified with hydrochloric acid, extracted with ether three times, etc. Concentration and distillation of the dried and neutral ether phase gave 12.5 g of diethyl phenyl cyanoacetate, 113–115°C/0.1 mm Hg, $n_D^{20} = 1.5048$.

SUMMARY

Sadeh and Berger have unsuccessfully attempted to prepare ethyl acetoxy cyanoacetate from ethyl bromocyanoacetate and potassium acetate and from lead tetraacetate and ethyl cyanoacetate. It has now been shown that benzoyl peroxide, when allowed to react with the sodium compound or ethyl cyanoacetate in benzene, gives both the benzoyloxy and dibenzoyloxy derivatives of ethyl cyanoacetate. By modifying the procedure, ethyl benzoyloxy cyanoacetate is obtained in 60% yield. A representative series of alkyl, aryl, and aralkyl substituted cyanoacetic esters have been shown to react in a similar way and enough data have been collected to show that the reaction may be generalized. It is postulated that the rupture of the oxygen–oxygen bond occurs by nucleophilic attack, e.g. by an ionic-type mechanism, and the conventional free-radical mechanism is rejected.

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To Professor A. Fredga, the Head of this Institute, we wish to express our sincere gratitude for the facilities put at our disposal and for his interest in this work. Grants from the *Swedish Natural Science Research Council* and *Lucidol Division, Wallace and Tiernan, Inc., Buffalo, N.Y.* are gratefully acknowledged.

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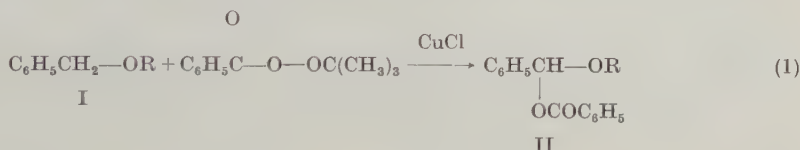
Uppsala 1961. Almqvist & Wiksells Boktryckeri AB

Studies on peroxy compounds

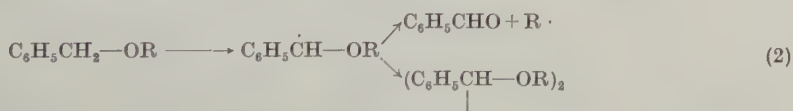
XIV. The reaction of benzaldehyde dialkylacetals with free radicals¹

By SVEN-OLOF LAWESSON and TAMARA BUSCH

In our work on the copper salt catalyzed decomposition of *t*-butyl perbenzoate in the presence of ethers, it was found that a benzyl ether, I, smoothly gives an α -benzoyloxy compound II according to the following [1, 2]:



With dibenzyl ether (I, R = C₆H₅CH₂) no acylal II was isolated but benzaldehyde dibenzylacetal and benzaldehyde were found. It was concluded that the copper salt had a stabilizing effect on the intermediate benzyl radical (C₆H₅CH—OR), which is a reasonable postulate as Huang *et al.* [3], by decomposing *t*-butyl peroxide in the presence of I, observed fragmentation, dimerization or both according to the following scheme:

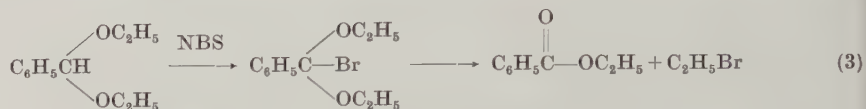


A simple ether such as di-*n*-butyl ether, does not seem to undergo any fragmentation, and, in connection with our current interest in free-radical reactions with ethers, we have made a series of experiments with acetals of benzaldehyde in an attempt to elucidate the encountered problems with dibenzyl ether (see above).

To our knowledge, reactions of acetals and similar compounds under radical conditions have earlier been reported in the literature only to an exploratory extent. Methylal reacts with maleic anhydride to give a 1:1 product [4], and 1,3-dioxane or dioxalanes similarly add to α,β -unsaturated esters [5]. A survey of the literature further reveals that bromination of acetals with *N*-bromosuccinimide gives the α -bromoacetal and other product(s) with a more active bromine [6]. It was postulated without proof, that bromination occurred on the carbon containing the two ether

¹ Part XIII. Lawesson, S.-O., and Frisell, C., Arkiv Kemi 17, 409 (1961).

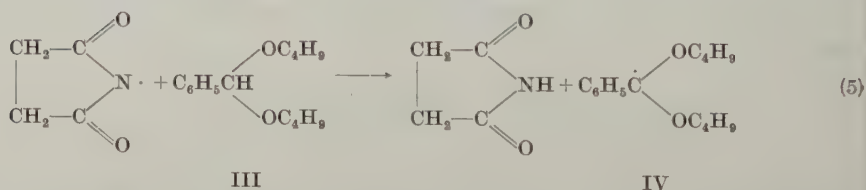
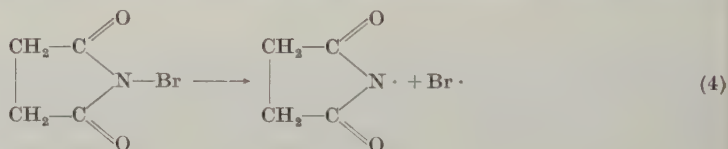
linkages. Further, bromination of benzaldehyde diethylacetal only gave ethyl benzoate and, although ethyl bromide was not isolated, a mechanism was postulated as follows:



Finally, two recent and more thorough investigations should be mentioned which deal with reactions of *t*-butyl peroxide and 2-methoxytetrahydropyran [7] and aliphatic acetals [8], respectively.

Benzaldehyde di-*n*-butylacetal was treated with *N*-bromosuccinimide (NBS) under conditions which did not prevent a free-radical reaction. The only products detected were *n*-butyl benzoate and *n*-octane, and no *n*-butyl bromide or aldehyde were found. Benzaldehyde dibenzylacetal was similarly reacted with NBS in carbon tetrachloride. Benzyl benzoate was isolated, and a fraction was obtained which was shown to contain an aldehyde using IR; further, due to the lachrymatory nature of the mixture, a reactive halide of benzylic type was also thought to be present. As we were unsuccessful in separating the postulated compounds, benzaldehyde and benzyl bromide, the mixture was treated with magnesium in ether according to Grignard and gave benzyl phenyl carbinol, which proved that the supposed compounds were present.

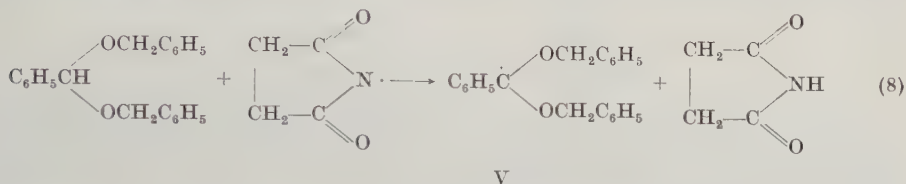
We can account for the different products in the following way: it is known that *N*-bromosuccinimide reacts according to a radical chain mechanism [eqn 4] and the



abstraction of the hydrogen of the benzaldehyde dibutylacetal occurs according to eqn. 5.

The intermediate radical IV undergoes fragmentation according to eqn. 6, giving *n*-butyl benzoate and butyl radicals, the latter dimerizing to *n*-octane (eqn. 7). As no aldehyde was found, no attack on the acetal other than that indicated, seems to have taken place. The bromine radicals are finally supposed to give bromine.

In the case of benzaldehyde dibenzylacetal, additional reactions are proposed to explain the different fragments formed. First, as with benzaldehyde dibutylacetal, a hydrogen is removed:



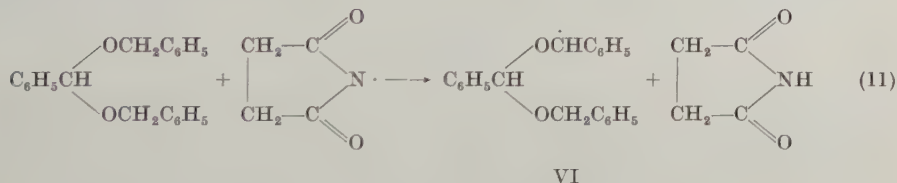
Fragmentation according to the general scheme gives the following:



and the benzyl radicals, stabilized by resonance, do not dimerize but with bromine radicals give benzyl bromide:

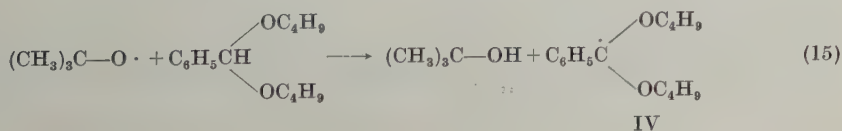


To explain the formed benzaldehyde, the succinimide radical is supposed to attack the methylene group as follows:

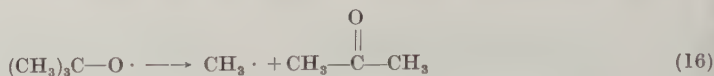


Fragmentation occurs according to eqn. 12 followed by another fragmentation (eqn. 13) and benzyl bromide is finally generated according to eqn. 10.

Benzaldehyde dibutylacetal was also reacted with *t*-butylperoxide at 125–150°C and the products found were *n*-butyl benzoate, *t*-butanol and *n*-octane. It is quite clear that the *t*-butoxy radical formed according to eqn. 14 removes a hydrogen from

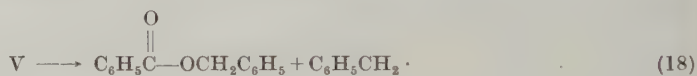


the acetal (eqn. 15) giving the intermediate radical IV, which then fragments according to eqn. 6; the formation of *n*-octane follows from eqn. 7. Further, it is known that *t*-butoxy radicals can decompose into methyl radicals and acetone (eqn. 16)

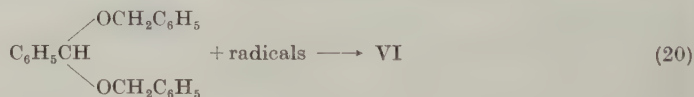


and it is therefore not unlikely that part of the hydrogen abstraction (eqn. 15) is done by methyl and *n*-butyl radicals, too.

When benzaldehyde dibenzyl acetal was heated with *t*-butyl peroxide, the following products were found: benzyl benzoate, dibenzyl, benzaldehyde and meso-dihydrobenzoin-dibenzoate. Benzylbenzoate and bibenzyl are formed as follows:

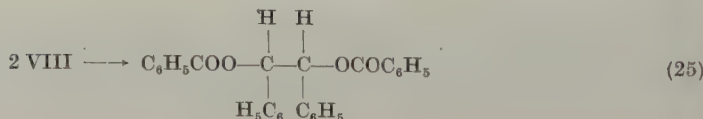
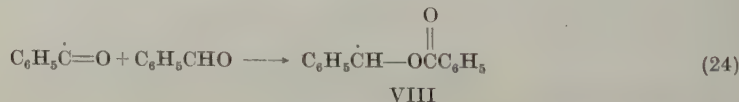
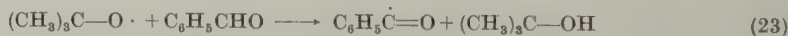


To account for the other products, it is postulated that abstraction of hydrogen occurs at the methylene group, giving the intermediate radical VI (eqn. 20) which

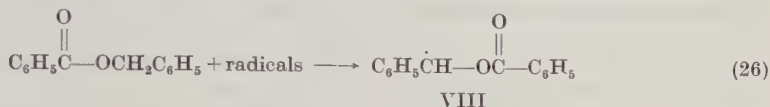


undergoes fragmentation in two steps (eqns. 21 and 22); dibenzyl is formed according to eqn. 19.

Finally, meso-dihydrobenzoin dibenzoate is formed as follows [9]

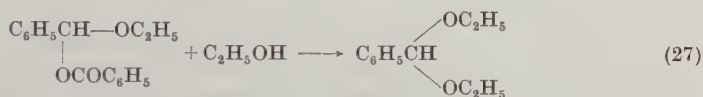


An alternative route to meso-dihydrobenzoin dibenzoate is from the formed benzyl benzoate as follows:



followed by dimerization of VIII (eqn. 25),

In connection with our findings from the reactions between benzaldehyde dibenzylacetal and radicals, we might refer to the recent investigation by Lawesson and Berglund [2] in which dibenzyl ether (I, R = benzyl) was heated with *t*-butyl perbenzoate in the presence of cuprous chloride and the only products isolated were benzaldehyde dibenzyl acetal and benzaldehyde. No acylal (II) was found, although it was postulated that II (R = benzyl) existed as a primary product. As it has been shown that an alkyl-oxygen heterolysis is possible in the following case (eqn. 27), the formation



of benzaldehyde dibenzyl acetal might be explained in a similar way. To account for the benzaldehyde isolated [2], it might be supposed that the radical VI is an intermediate which, in spite of the cuprous chloride present, undergoes fragmentation.

The result of the bromination of an acetal with NBS may be best accounted for by eqns. 4-7.

Experimental

The reactions described were carried out in an oxygen-free nitrogen atmosphere from which moisture was excluded. All starting materials were purified prior to use. Commercial *N*-bromosuccinimide (NBS)¹ and di-*t*-butyl peroxide (Schuchardt) were used in all experiments. The infrared spectra were recorded on an Infracord.

Starting material

The benzaldehyde di-*n*-butylacetal (b.p. 140-145°/10 mm Hg; $n_D^{20} = 1.4770$) and benzaldehyde dibenzylacetal (b.p. 170°/0.2 mm Hg; $n_D^{20} = 1.5776$) were prepared by heating benzaldehyde and the corresponding alcohol in the presence of hydrochloric acid.

Reaction between NBS and benzaldehyde di-*n*-butylacetal

37 g (0.16 mole) of benzaldehyde di-*n*-butylacetal and a trace of benzoyl peroxide in 150 ml of carbon tetrachloride are placed in a flask with a mechanical stirrer and reflux condenser. 28.5 g (0.16 mole) of NBS was added but the reaction did not start immediately. However, after heating to 55-65°C for 15 minutes, the reaction started and the solution became yellow. After stirring overnight, the succinimide was filtered off under suction and the carbon tetrachloride solution, diluted with 100 ml of ether, was shaken once with a saturated solution of sodium carbonate, and then washed until neutral with water and dried over sodium sulphate. Distillation gave a first

¹ Generously supplied by Arapahoe Chemicals, Inc., Boulder, Colorado.

fraction, b.p. 70–105°C, and 17 g of *n*-butyl benzoate, b.p. 118–122°C/12 mm Hg; $n_D^{20} = 1.4985$ – 1.4987 , identical in all respects with authentic butyl benzoate.

The first fraction was analyzed by VPC and shown to contain carbon tetrachloride and *n*-octane.

Reaction of NBS with benzaldehyde dibenzylacetal

To 90.2 g (0.3 mole) of benzaldehyde dibenzylacetal and 150 ml of dry carbon tetrachloride with traces of benzoyl peroxide, 53.7 g (0.3 mole) of NBS are added in portions. The reaction is very slow but after gentle heating to 50–55°C for 25 minutes an exothermic reaction starts. The mixture is stirred at room temperature for 12 hours and is then worked up. The succinimide is filtered off using suction; the organic phase shaken with saturated sodium bicarbonate solution for 30 minutes, washed free of base with water, and dried over sodium sulphate. Distillation gave about 60 g of a mixture of benzyl bromide and benzaldehyde (the Beilstein test was positive and in the infrared a distinct absorption at 1700 cm^{-1} was observed; the fraction was also extremely lachrymatory) with b.p. 65–72°C/12 mm Hg; $n_D^{20} = 1.5685$ and 6 g of benzyl benzoate with b.p. 132–135°C/0.4 mm Hg, identical with an authentic sample of benzyl benzoate. In order to show more definitely that the lower-boiling fraction was a mixture of benzyl bromide and benzaldehyde, a sample (20 g) in 50 ml of dry ether was added to 5 g of magnesium turnings covered with 50 ml of dry ether. A violent reaction started and after it had subsided the work-up was made in the usual way. A solid precipitated after concentration; recrystallization from pet. ether gave white needles with m.p. 65–67°C and with authentic benzyl phenyl carbinol there was no depression of the mixed melting point.

*The reaction of *t*-butyl peroxide with benzaldehyde di-*n*-butylacetal*

In a flask fitted with a reflux condenser 23.6 g (0.1 mole) of benzaldehyde di-*n*-butylacetal and 8.0 g of *t*-butyl peroxide are placed. Oxygen-free nitrogen is flushed through the flask, which is then immersed in an oil bath at 135°C. Reflux under nitrogen is continued for 72 hours. Distillation gave 10.4 g of lower-boiling material (*t*-butanol, *n*-octane) b.p. < 30°/10 mm Hg and 23.5 g of a crude product with b.p. 118–140°C/10–15 mm Hg; redistillation gave 14.9 g of *n*-butyl benzoate, b.p. 118°/10 mm Hg, $n_D^{20} = 1.4986$, identical in all respects with authentic *n*-butyl benzoate.

*Reaction of benzaldehyde dibenzylacetal with *t*-butyl peroxide*

30.4 g (0.1 mole) of benzaldehyde dibenzylacetal and 8 g of *t*-butyl peroxide are placed in a flask with a reflux condenser and the mixture is heated under nitrogen for 72 hours in an oil bath at 120–130°C. Distillation gave a fraction 1, which mostly consisted of *t*-butyl alcohol (b.p. 20–60°C/10–20 mm Hg); fraction 2 (2.1 g) with b.p. 60–65°C/10 mm Hg, $n_D^{20} = 1.5482$ was identified as benzaldehyde; fraction 3, b.p. 86–106°C/0.07 mm Hg weighed 0.8 g and crystallized in the refrigerator after standing; recrystallization from pet. ether gave needles with m.p. 50–52°C, mixed m.p. with dibenzyl 50–52°C; fraction 4 consisted of 3.4 g of benzyl benzoate, b.p. 130–135°/0.4 mm Hg, $n_D^{20} = 1.5680$, and whose IR-spectrum and that of authentic benzyl benzoate were superimposable; fraction 5 was 11 g of the starting material benzaldehyde dibenzyl acetal; from the residue, which was first dissolved in benzene, a white powder precipitated by addition of pet. ether which upon recrystallization from ether + pet. ether gave white crystals with m.p. 246°C; a mixed m.p. with meso-dihydrobenzoin dibenzoate was not depressed.

SUMMARY

Two acetals of benzaldehyde have been allowed to react with *t*-butyl peroxide and *N*-bromosuccinimide. In both cases esters of benzoic acid were isolated as main products, and attempts to explain the observed fragmentations have been made.

ACKNOWLEDGEMENTS

The authors are indebted to Professor A. Fredga, Head of this Institute, for facilities put at their disposal and for his kind interest in this work. Grants from *Magnus Bergwalls stiftelse* and *Lucidol Division, Wallace and Tiernan, Inc, Buffalo, N.Y.* are gratefully acknowledged.

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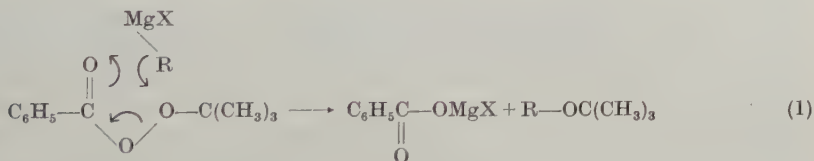
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Tryckt den 4 maj 1961

Uppsala 1961. Almqvist & Wiksells Boktryckeri AB

XV. The introduction of the *t*-butoxy and benzyloxy groups into β -ketoesters. A method for the preparation of α -hydroxyesters¹

Denney and his associates and Walling and co-worker have, during recent years, investigated the reaction between benzoyl peroxide and phenols [1], amines [2] and phosphines [3] and postulated that the nucleophilic reagents attack the oxygen-oxygen bond (the weakest in the peroxide) and thus the benzoyloxy group is primarily introduced into the corresponding substrate. Investigations have been made by us on the reaction between sodium derivatives of so-called active methylene compounds and certain peroxides in which the oxygen-oxygen bond is also broken. This investigation was initiated by the finding of Lawesson and Yang [4] that a Grignard reagent and *t*-butyl perbenzoate under very mild conditions readily gives the *t*-butyl ether; this reaction, if the symbol RMgX is not taken too literally, may be formulated as



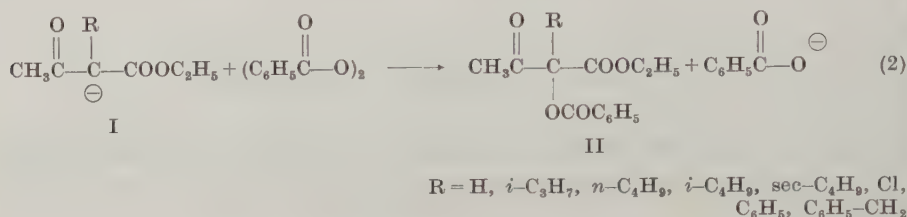
It was thus thought that certain sodium derivatives would react similarly with peresters but this was not the case, only small yields of *t*-butoxy compounds being obtained, for example from the reaction between *t*-butyl peracetate and diethyl malonate or ethyl acetoacetate [5]. However, it was found that benzoyl peroxide readily reacts giving the corresponding benzoyloxy compound [6-8]; the generality of these observations is being examined.

Extensive modifications to the original procedure [5] for introducing the *t*-butoxy group into ethyl acetoacetate have been tried but met with no success. Attempts

¹ Part XIV. Lawesson, S.-O., and Busch, T., *Arkiv Kemi* 17, 421 (1961).

with substituted β -ketoesters were also futile, and no further efforts are planned as the first-found method seems to be of a limited value.

The reaction between benzoyl peroxide and ethyl acetoacetate and its derivatives did not show any deviations from the general pattern. No gases were evolved and, generally, excellent yields of benzoyloxy derivatives were found. The stoichiometry of the reaction is as follows



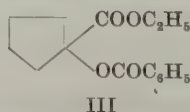
The benzoyloxy derivatives, II, are all stable for at least one year and are very viscous as liquids.

The procedure did not vary from that earlier described, that is, the sodium compound was prepared from the β -ketoester and sodium hydride in benzene. This is generally a fast reaction and to the cooled mixture benzoyl peroxide, dissolved in benzene, is added. An excess of the sodium compound was always used and in many cases all the peroxide was consumed. If this is not the case, peroxides may be easily destroyed by shaking the solution with sodium iodide in glacial acetic acid.

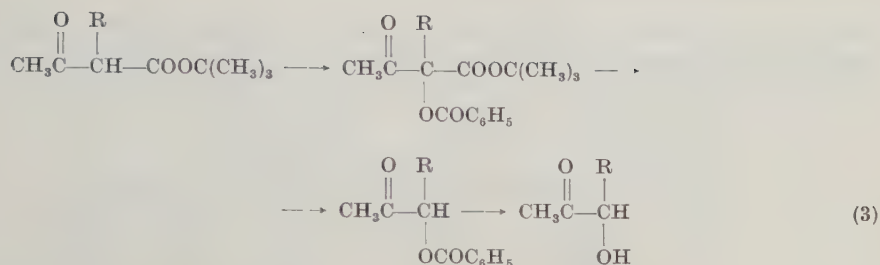
As far as is known, no benzoyloxy derivative of ethyl acetoacetate is recorded in the literature. However, acetoxy groups have been introduced; Dimroth *et al.* [9] treated ethyl acetoacetate with lead tetracetate, whereby the α -acetoxy derivative was formed, and lately a few substituted ethyl acetoacetates have been found to react similarly [10]. Another method is to start from ethyl α -chloroacetoacetate which, when treated with potassium acetate in acetic anhydride, gives the same type of compound [11, 12].

It is also seen from eqn. 2 that ethyl α -chloro acetoacetate gives the corresponding benzoyloxy derivative II (R=Cl), indicating that the sodium compound of ethyl α -chloro acetoacetate is formed in benzene without any dechlorination and that the reaction with benzoyl peroxide runs readily. The chloro-atom in II (R=Cl) may be eliminated using a Grignard reagent which is a very convenient method as the ester groups are not attacked. It is clear that Grignard reagents add slowly to any of the carbonyl groups in II (R=Cl) possibly due to steric hindrance.

Besides benzoyloxy compounds in the ethyl acetoacetate series, we also prepared a benzoyloxy compound from 2-carbethoxy cyclopentanone. This compound, III, did not seem to be as stable to heat as II and some decomposition was observed in the final distillations.

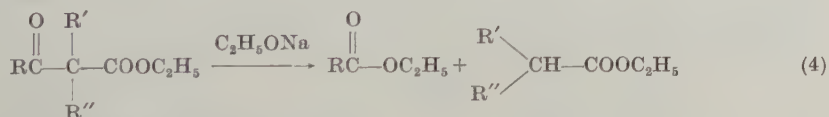


As Lawesson, Grönwall and Andersson [13, 14] recently prepared acyloins according to eqn. 3, it would be quite natural to attempt ketone cleavage of α -benzoyloxy

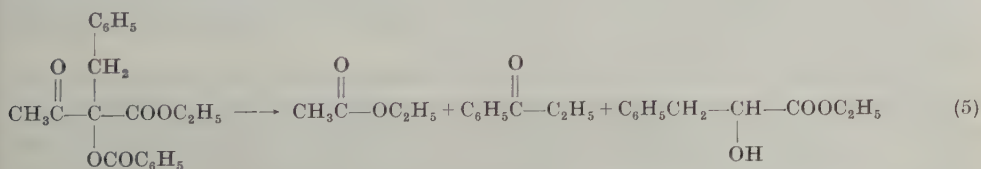


derivatives (II), which would give acyloins as the final products. However, it was unsuccessful as the different ethyl benzoyloxy acetoacetates investigated were found to be very stable to acid: a 40% sulphuric acid solution did not cause any decomposition when heated with the ester for 4–5 hours at gentle reflux. Nor did mild treatment with a base convert II into acyloins. When stronger acid was used, fragmentation occurred but the formed products were simultaneously destroyed. The benzoyloxy derivatives apparently differ to a certain extent from the corresponding acetoxy compounds, however. Böhme and Schneider [15] studied different methods of preparing ethyl α -hydroxy acetoacetate [16, 17] and were successful on treating ethyl acetoxy acetoacetate with dilute hydrochloric acid at room temperature for 18 hours. Using the same conditions, but extending the reaction time to a week, we attempted to hydrolyze II ($\text{R} = \text{H}$) but all starting material was recovered unchanged.

As cleavage of the β -ketoester, II, with acids as bases seemed to be impossible we treated the esters with sodium alcoholate; this is the method first worked out by Adkins [16]:

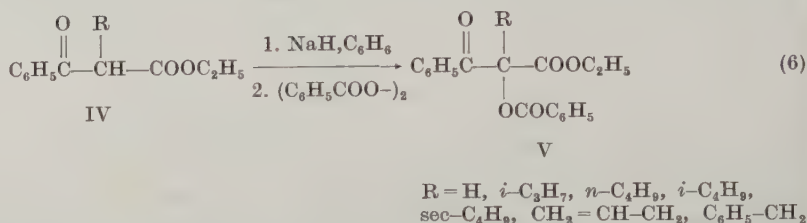


However, with benzoyloxy derivatives a certain complication is encountered as the nucleophilic reagent can attack the benzoyl and/or acetyl groups.



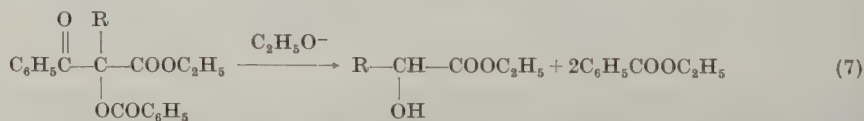
From eqn. 5 it is seen which products are obtained from alcoholysis of ethyl benzyl benzoyl acetoacetate. In this case, ethyl α -hydroxy- β -phenyl propionate could be separated by distillation from ethyl benzoate but with II ($\text{R} = n\text{-C}_4\text{H}_9$), the products could not be successfully fractionated. It is therefore concluded that α -hydroxy esters can be easily prepared from ethyl benzoyloxy acetoacetates by alcoholysis, but that difficulties with the separation, due to the small differences in boiling point between ethyl benzoate and the new hydroxy ester, limits the utility of the method.

Besides the synthesis of α -benzoyloxy derivatives of ethyl acetoacetates and 2-carbethoxy cyclopentanone, we have also prepared a series of derivatives (V) from ethyl benzoylacetates (IV).



To get IV to react with sodium hydride, heat had generally to be applied but the succeeding reaction with benzoyl peroxide ran smoothly without gas evolution. Quantitative yields of benzoic acid were found but difficulties were encountered with the final purifications of the benzoate V. In three cases ($\text{R} = \text{H}$, allyl, benzyl), crystalline products were isolated in high yields but otherwise certain resinification occurred during the distillations as the boiling points of most products were close to $170^\circ\text{C}/0.05 \text{ mm Hg}$. V ($\text{R} = \text{Cl}$) decomposed when distilled and only acidic products were found.

Like the benzoyloxy derivatives II, V was also very stable to acid or base and it was further observed that, if too mild conditions were applied, the starting compounds were recovered, whereas with more vigorous hydrolysis destruction of all products occurred. Alcoholysis with sodium alkoxide in ethyl alcohol gave ethyl benzoate and hydroxy esters, indicating that both benzoyl groups were attacked by the species $\text{C}_2\text{H}_5\text{O}^-$.



In a paper by Bradley and Robinson [17]¹ it was found that a few experiments had been done with benzoyl peroxide and some β -ketoesters; V ($\text{R} = \text{H}$) had been prepared and also found to be very resistant to hydrolysis.

Concerning the mechanism of the reaction between benzoyl peroxide and sodium compounds of active methylene compounds, we have, in the case of malonates [7] and cyanoacetates [8], postulated the exclusion of a conventional free-radical mechanism. A nucleophilic attack on the oxygen-oxygen bond is more plausible considering earlier work on phenols, amines and phosphines [1-3]. Work is in progress with benzoyl peroxide (carbonyl O^{18}).

¹ Civ.ing. J. Taipale, Helsinki, Finland, has kindly drawn the authors' attention to this paper.

$$\begin{array}{c} \text{O} \quad \text{R} \\ || \quad | \\ \text{CH}_3\text{C}-\text{CH}-\text{COOC}_2\text{H}_5 \end{array}$$
 Table 1. Physical constants of

R	B.p. (°C)	mm Hg	n_D^{20}	Ref.
<i>i</i> -C ₃ H ₇	92	20	1.4275	18
<i>n</i> -C ₄ H ₉	115	16	1.4288	19
<i>i</i> -C ₄ H ₉	96-98	12	1.4290	20
sec-C ₄ H ₉	98-101	15	1.4332	21
C ₆ H ₅ -CH ₂	159-160	13	1.5017	22
Cl	115-116	50	1.4438	23

Experimental

The reactions between benzoyl peroxide and the corresponding sodium derivatives were performed in an atmosphere from which moisture was excluded. Benzoyl peroxide was recrystallized at low temperature from methanol and chloroform; *t*-butyl peracetate was supplied by Lucidol Division, Wallace and Tiernan, Inc., Buffalo. Experiments with Grignard reagents were run in a common assembly. The infrared curves were recorded on an Infracord. The analysis was made by Dr. Alfred Bernhardt, Mülheim (Ruhr) and the Analytical Department of Uppsala University. Boiling and melting points are uncorrected.

Starting material

The alkylsubstituted β -ketoester were prepared according to known methods. The physical constants are given in Tables 1 and 2 and the procedure is given in detail for two new compounds.

Preparation of ethyl *n*-butyl benzoylacetate

In a 500 ml three-necked flask with stirrer, condenser and dropping-funnel, 0.25 mol of sodium alcoholate was prepared from 5.75 g (0.25 mole) of sodium and 125 ml of ethyl alcohol. Then 48.5 g (0.25 mole) of ethyl benzoylacetate were added dropwise. 35.5 g (0.26 mole) of *n*-butyl bromide were added and the whole mixture refluxed

$$\begin{array}{c} \text{O} \quad \text{R} \\ || \quad | \\ \text{C}_6\text{H}_5\text{C}-\text{CH}-\text{COOC}_2\text{H}_5 \end{array}$$
 Table 2. Physical constants of

R	B.p. (°C)	mm Hg	n_D^{20}	Ref.
<i>i</i> -C ₃ H ₇	112-115	0.6	1.5118	24
<i>n</i> -C ₄ H ₉	114	0.4	1.5044	
<i>i</i> -C ₄ H ₉	153-155	11	1.5100	24
sec-C ₄ H ₉	125-127	0.8	1.5091	
allyl	127	1.5	1.5201	25
C ₆ H ₅ CH ₂	165-167	0.6	1.5569	26
Cl	126-127	0.4	1.5330	27

for 2½ hours (the solution had become almost neutral). Most of the alcohol was immediately removed, water added and the water phase extracted with ether 3–4 times. The combined extracts were washed free from base, dried, concentrated and distilled. The main fraction boiled at 114°C/0.4 mm Hg, $n_D^{20} = 1.5044$. Yield 40.4 g (84 %).

Anal. Calc. C 69.10, H 5.86

Found C 69.00, H 5.73

Preparation of ethyl sec-butyl benzoylacetate

Sodium alcoholate was prepared from 5.75 g (0.25 mole) of sodium and 125 ml of ethanol and 48.05 g (0.25 mole) of ethyl benzoylacetate were added dropwise. The solution was heated to 80°C and 37.5 g (0.27 mol) of sec-butyl bromide were added; after the mixture had refluxed for 46 hours it was almost neutral. After being worked up in the usual way, distillation gave a main fraction with b.p. 124–127°C/0.8 mm Hg, $n_D^{20} = 1.5091$. Yield 39.8 g (83 %).

Anal. Calc. C 69.10, H 5.80

Found C 69.11, H 5.77

Preparation of ethyl α -t-butoxy acetoacetate

The sodium compound of ethyl acetoacetate was prepared, in the usual way, from 6 g of sodium hydride and 30 g of the ester in 700 ml of benzene.

0.15 mol (38 ml) of *t*-butyl peracetate (Lupersol #7) was added but no reaction was observed. After heating gently an exothermic reaction started; after it had subsided, heat was applied again for 6 hours (60–70°C). The solution was poured out into water, the organic phase separated, the aqueous phase extracted four times with ether, and the combined extracts washed until neutral with water and finally dried over sodium sulphate. Distillation gave a pre-fraction of ethyl acetoacetate and a fraction with b.p. 78–80°C/1 mm Hg. Redistillation gave a pure fraction, b.p. 77–79°C/1 mm Hg, $n_D^{20} = 1.4292$. Weight 9.1 g (30 %).

Anal. Calc. C 59.38, H 8.97

Found C 59.47, H 8.85

Preparation of ethyl α -benzoyloxy acetoacetate

In a three-necked flask, with stirrer, dropping-funnel and reflux-condenser, and containing 3.6 g of sodium hydride and 150 ml of dry benzene, 19.5 g (0.15 mol) of ethyl acetoacetate were added dropwise and a gray-white porridge-like mass formed to which another 200 ml of benzene were added. After 4½ hours, all the sodium hydride had been consumed. The mixture was cooled in an ice-bath to zero and 30.2 g (0.125 mole) of benzoyl peroxide in 360 ml of benzene were added for 70 minutes. No gas was collected. Stirring was continued overnight and the mixture was then poured into water. The benzene phase was separated, the water phase twice extracted with ether, the organic layers combined, washed until neutral with water, and dried over sodium sulphate. The solvents were removed and distillation gave the main fraction with b.p. 124–125°C/0.3 mm Hg, $n_D^{20} = 1.5048$. Yield 15.4 g (41 %).

Anal. Calc. C 62.39, H 5.64

Found C 62.31, H 5.63

From the water phase 16.4 g of benzoic acid was isolated.

Ethyl i-propyl benzoyloxy acetoacetate

The sodium compound was prepared from 3.6 g (0.15 mole) of sodium hydride covered with 180 ml of dry benzene and 31.2 g (0.18 mole) of ethyl iso-propyl acetoacetate added. A gray-white precipitate was formed, insoluble in benzene. The mixture, to which another 80 ml of benzene had been added, was cooled and 25 g (0.103 mole) of benzoyl peroxide dissolved in 225 ml of benzene were added for 75 minutes. The mixture was stirred for 12 hours, poured into water and worked up as above. Isolated benzoic acid 12.5 g; distillation gave the main fraction with b.p. 135–136°C/0.3 mm Hg, $n_D^{20} = 1.4979$. Yield 22.2 g (74 %).

Anal. Calc. C 65.74, H 6.90
Found C 65.75, H 7.04

Ethyl n-butyl benzoyloxy acetoacetate

To 3.6 g (0.15 mole) of sodium hydride, covered with 150 ml of dry benzene, 28.1 g (0.15 mole) ethyl n-butyl acetoacetate were added dropwise. Some heat was applied so that all hydride was consumed. A yellow, very viscous liquid was obtained. After cooling, 24.2 g of benzoyl peroxide dissolved in benzene was added for 45 minutes. The mixture was stirred overnight and then worked up as above. Isolated benzoic acid 8.1 g. Distillation gave the main fraction with b.p. 145–148°C/0.4 mm Hg, $n_D^{20} = 1.4892$. Yield 16.5 g (54 %).

Anal. Calc. C 66.65, H 7.24
Found C 66.75, H 7.30

Ethyl iso-butyl benzoyloxy acetoacetate

The sodium derivatives was prepared from 3.6 g (0.15 mole) of sodium hydride in 150 ml of benzene to which 28.1 g (0.15 mole) of ethyl iso-butyl acetoacetate was added dropwise. A clear yellow solution was obtained. After cooling, 24.2 g (0.1 mole) of benzoyl peroxide in 300 ml of benzene were added for 65 minutes. The mixture was stirred overnight and worked up as above. 13.8 g of benzoic acid were isolated and the main fraction boiled at 142–143°C/0.5 mm Hg, $n_D^{20} = 1.4969$. Yield 23.6 g (77 %).

Anal. Calc. C 66.65, H 7.24
Found C 66.58, H 7.32

Ethyl sec-butyl benzoyloxy acetoacetate

21.0 g (0.11 mole) of ethyl sec-butyl acetoacetate were added to 2.6 g (0.11 mole) of sodium hydride covered with 100 ml of benzene; the sodium derivatives was insoluble in benzene. After cooling the mixture, 18.2 g (0.075 mole) of benzoyl peroxide in 350 ml of benzene was slowly added. The mixture was stirred overnight and then worked up. A quantitative yield of benzoic acid was found and by distillation the main fraction had b.p. 139–140°C/0.1 mm Hg, $n_D^{20} = 1.4989$. Yield 19.5 g (85 %).

Anal. Calc. C 66.65, H 7.24
Found C 66.60, H 7.23

Ethyl benzyl benzoyloxy acetoacetate

The sodium derivative (insoluble in benzene) was prepared from 3.6 g (0.15 mole) of sodium hydride in 150 ml of benzene and 33 g (0.15 mole) of ethyl benzyl acetoacetate. 24.2 g (0.1 mole) of benzoyl peroxide in benzene was added for 70 minutes and

the mixture stirred overnight and worked up as above. A quantitative yield of benzoic acid was obtained. Distillation gave the main fraction with b.p. 180–182°C/0.7 mm Hg, $n_D^{20} = 1.5282$. After some time it crystallized and recrystallization from pet. ether gave white crystals, m.p. 74–75°C. Yield 32.1 g (94 %).

Anal. Calc. C 70.57, H 5.92

Found C 70.46, H 5.93

Ethyl chloro benzoyloxy acetoacetate

The sodium compound was prepared at room temperature from 4.5 g (0.18 mole) of sodium hydride in 180 ml of benzene and 30.2 g (0.18 mole) of ethyl chloro acetoacetate. After three hours all hydride had been consumed and to the porridge-like mass 35 g (0.14 mole) of benzoyl peroxide in 280 ml of benzene were added. The mixture was stirred overnight and worked up as above; 15.9 g of benzoic acid was isolated. Distillation gave a main fraction with b.p. 117–119°C/0.06 mm Hg, $n_D^{20} = 1.5108$. Yield 20.7 g (52 %).

Anal. Calc. C 54.84, H 4.60

Found C 55.34, H 4.70

Dechlorination of ethyl chloro benzoyloxy acetoacetate

Ethylmagnesium bromide was prepared from 2 g of magnesium and 9 g of ethyl bromide in 50 ml of ether. The Grignard reagent was slowly added to 22.0 g of ethyl chloro benzoyloxy acetoacetate, cooled to zero. The mixture was stirred overnight and the mixture then poured out into water + hydrochloric acid. The ether layer was separated, the water phase extracted with ether many times and the combined ether extracts washed free of acid, dried and distilled. The main fraction, b.p. 132–134°C/0.4 mm Hg, $n_D^{20} = 1.5046$. Yield 12.7 g (66 %) was identical with ethyl benzoyloxy acetoacetate.

2-Benzoyloxy-2-carboethoxy-cyclohexanone

The sodium compound was prepared from 4.8 g (0.2 mole) of sodium hydride (in 200 ml of benzene) and 31.2 g (0.2 mole) of 2-carboethoxy cyclohexanone. The mixture (sodium derivative insoluble in benzene) was cooled to zero and 32 g (0.13 mole) of benzoyl peroxide dissolved in 250 ml of dry benzene was added for 50 minutes. The mixture was stirred for an hour and then worked up as above; 17.4 g of benzoic acid were isolated and the main product boiled at 136–140°C/0.05 mm Hg, $n_D^{20} = 1.5191$. Yield 29.6 g (82 %).

Anal. Calc. C 65.21, H 5.84

Found C 65.21, H 5.83

Alcoholysis of ethyl benzyl benzoyloxy acetoacetate

34 g (0.1 mole) of ethyl benzyl benzoyloxy acetoacetate and 150 ml of absolute ethyl alcohol were placed in a flask. An alcoholate solution, prepared from 4.6 g of sodium and 100 ml of absolute ethyl alcohol, was added dropwise to the mixture with violent stirring and it was then gently refluxed for 4½ hours. A rather viscous porridge-like solution was the result and a smell of ethyl acetate was observed. Part of the alcohol was stripped off at reduced pressure and the residue poured into water and extracted many times with ether. The extracts were combined, washed until

neutral with water, dried, concentrated and distilled. Two fractions were obtained: (1) Ethyl benzoate, b.p. 85°C/10 mm Hg, $n_D^{20} = 1.5062$. Yield 9.1 g. (2) Ethyl α -hydroxy- β -phenyl propionate, b.p. 87°C/04 mm Hg, $n_D^{20} = 1.5101$. Yield 11.9 g (64 %).

Anal. Calc. C 68.02, H 7.27

Found C 67.89, H 7.30

Ethyl α -hydroxy- β -phenylpropionate was refluxed with hydrochloric acid for 1½ hours and then poured into water, followed by extraction with ether. From the ether phase, α -hydroxy- β -phenyl propionic acid was isolated. Crystallization from benzene or pet. ether gave white needles, m.p. 97–99°C.

Anal. Calc. C 65.04, H 6.06

Found C 65.03, H 6.11

Preparation of ethyl benzoyloxy benzoylacetate

The sodium derivative was prepared from 2.4 g (0.1 mole) of sodium hydride in 100 ml of benzene and 19.2 g (0.1 mole) of ethyl benzoylacetate. After cooling the mixture, 20 g (0.083 mole) of benzoyl peroxide, dissolved in 200 ml of dry benzene, were added dropwise for 40 minutes. The mixture was stirred overnight and worked up as above. When the excess ethyl benzoylacetate had been distilled off, the residue solidified. Yield 18.5 g (72 %). After recrystallization from ether + pet. ether, white crystals were obtained with m.p. 60–61°C. (lit. [17] 61°C).

Anal. Calc. C 69.22, H 5.16

Found C 68.93, H 5.21

Ethyl i-propyl benzoyloxy benzoylacetate

The sodium derivative was made from 2.4 g (0.1 mole) of sodium hydride covered with 100 ml of benzene and 23.4 g (0.1 mole) of ethyl *i*-propyl benzoylacetate. Heat was applied until all hydride had been used up and a clear yellow solution was formed. 18 g (0.074 mole) of benzoyl peroxide in 250 ml of benzene was added to the cooled solution for an hour. The mixture was stirred overnight and then worked up. A quantitative yield of benzoic acid was isolated. Distillation gave the main fraction with b.p. 165–167°C/0.05 mm Hg, $n_D^{20} = 1.5498$. Yield 11.3 g (43 %).

Anal. Calc. C 71.17, H 6.26

Found C 71.29, H 6.48

Ethyl n-butyl benzoyloxy benzoylacetate

The sodium compound was prepared from 2.4 g (0.1 mole) of sodium hydride in 100 ml of benzene and 24.8 g (0.1 mole) of ethyl *n*-butyl benzoylacetate. This reaction was sluggish and heat was applied to all the hydride consumed. 18 g (0.074 mole) of benzoyl peroxide in 200 ml of dry benzene were added to the cooled, clear solution for 65 minutes. The mixture was stirred overnight and then worked up as above (9.4 g of benzoic acid were isolated) 18.4 g (67 %) of the product were obtained with b.p. 172–173°C/0.05 mm Hg, $n_D^{20} = 1.5399$.

Anal. Calc. C 71.72, H 6.57

Found C 71.78, H 6.54

Ethyl iso-butyl benzoyloxy benzoylacetate

The sodium compound was soluble in benzene and was prepared from 4 g (0.17 mol) of sodium hydride in 200 ml of benzene and 42 g (0.17 mole) of ethyl iso-butyl benzoylacetone; heat was applied. 30 g (0.12 mole) of benzoyl peroxide in 300 ml of benzene was added with cooling for 1 hour. The mixture was stirred overnight and worked up as above. The main fraction had a b.p. 183–186°C/0.1 mm Hg, $n_D^{20} = 1.5472$. Yield 17.3 g (39 %).

<i>Anal.</i> Calc.	C 71.72,	H 6.57
Found	C 71.70,	H 6.53

Ethyl sec-butyl benzoyloxy benzoylacetate

The sodium compound, prepared from 2.4 g (0.1 mole) of sodium hydride in 100 ml of benzene and 23.8 g (0.09 mole) of ethyl sec-butyl benzoylacetate, was cooled and 9 g (0.04 mole) of benzoyl peroxide in 100 ml of benzene were added for 50 minutes. The mixture was stirred overnight and worked up as above. The main fraction had b.p. 156–158°C/0.05 mm Hg, $n_D^{20} = 1.5420$. Yield 6.5 g (44 %).

<i>Anal.</i> Calc.	C 71.72,	H 6.57,
Found	C 71.72,	H 6.62

Ethyl allyl benzoyloxy benzoylacetate

The sodium compound, prepared from 4.8 g sodium hydride in 200 ml of benzene and 33.4 g (0.14 mole) of ethyl allyl benzoylacetate, was cooled in an ice-water bath and 24.2 g (0.1 mole) of benzoyl peroxide in benzene added; worked up as above. After the excess of starting material had been stripped off, the rest solidified. Recrystallization from pet. ether gave white crystals with m.p. 74–76°C. Yield 27.5 g (78 %). A quantitative yield of benzoic acid was isolated.

<i>Anal.</i> Calc.	C 71.58,	H 5.72
Found	C 71.60,	H 5.71

Ethyl benzyl benzoyloxy benzoylacetate

This compound was prepared as above from the corresponding sodium compound, prepared from 2.4 g (0.1 mole) of sodium hydride in 100 ml of benzene, 28.2 g (0.1 mole) of ethyl benzyl benzoylacetate, and 20 g (0.083 mole) of benzoyl peroxide in 250 ml of benzene. The product was a solid, which, after recrystallization from ether + pet. ether, gave white needles with m.p. 99–100°C. Yield 27.5 g (82 %).

<i>Anal.</i> Calc.	C 74.61,	H 5.51
Found	C 74.77,	H 5.61

Alcoholysis of ethyl benzyl benzoyloxy benzoylacetate

40.2 g (0.1 mole) of ethyl benzyl benzoyloxy benzoylacetate in 200 ml of absolute ethanol were placed in a flask. An alcoholate solution, prepared from 2.3 g (0.1 mole) of sodium in 100 ml of absolute ethanol, was added to the ester and heated for 4 hours. From the yellow viscous liquid, ethyl alcohol was stripped off at reduced pressure and water was added. Extraction with ether was made several times, the combined extracts washed until neutral with water, dried over sodium sulphate, concentrated, and distilled.

Fraction 1: b.p. 89–90°C/10 mm Hg, $n_D^{20} = 1.5065$ consisted of ethyl benzoate. Yield 18.3 g.

Fraction 2: b.p. 90–92°C/0.5 mm Hg, $n_D^{20} = 1.5097$ consisted of ethyl α -hydroxy- β -phenyl propionate. Yield 13.3 g (64%). Hydrolysis of the ester gave α -hydroxy- β -phenyl propionic acid, m.p. 97–99°C.

SUMMARY

The benzoyloxy group has been introduced into the α -position of different β -ketoesters using the benzoyl peroxide method. α -Hydroxy esters are obtained by alcoholysis of the benzoyloxy derivatives.

ACKNOWLEDGEMENTS

The authors are indebted to the Head of this Institute, Professor A. Fredga, for facilities put at their disposal and for his kind interest in this work. Grants from *Statens Naturvetenskapliga Forskningsråd* and *Lucidol Division, Wallace and Tiernan, Inc, Buffalo, N.Y.* are gratefully acknowledged.

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Studies on peroxy compounds

XVI. The preparation of benzoyloxy derivatives of β -diketones¹By SVEN-OLOF LAWESSON, PER-GUNNAR JÖNSSON and JYRKI TAIPALE²

As a sequel to recent work [1–6], the present paper concerns investigations of the reaction between benzoyl peroxide and sodium compounds of homologues of acetylacetone, benzoylacetone and a few cyclic β -diketones. The oxygen–oxygen bond of benzoyl peroxide is easily ruptured when a sodium compound of an active methylene compound in benzene is treated with purified benzoyl peroxide [7] and a high yield of a benzoate is generally obtained. Other methods of introducing acyloxy groups into β -carbonyl compounds are to treat them with lead tetraacetate [8] or to react a sodium carboxylate with the appropriate bromo- β -carbonyl compound [9]. With ethyl cyanoacetate, only the benzoyl peroxide method is successful [3] as the other methods either give unexpected products or only tar. As far as is known with β -diketones, no benzoyloxy derivatives (or acyloxy ones) have been prepared and, in order to explore the generality of the benzoyl peroxide method, this work has now been done.

It was found to be rather tedious to prepare the starting materials in the acetylacetone and benzoyl acetone series. There is a great difference, for instance, between malonic esters and β -diketones, the former being easily alkylated and the latter difficult to alkylate in most cases. Different methods are described in the literature, the highest yields having been obtained by first preparing the sodium compound, followed by alkylation with excess of alkyl iodide in acetone or dioxane [10]. In alcoholic solution, the yields of alkylated products were diminished [11]. Another alkylation method, giving high yields, is to heat the sodium compound with an excess of alkyl iodide in an autoclave at 150–250°C [12].

The method used in this work is a modification of the method first worked out by Weygand [11] and which was then used by Sprauge *et al.* The more convenient sodium hydride was used instead of sodium in our preparations, and in Tables 1 and 2, a comparison of our results with earlier findings is to be found. The products boiled over a wide range, which may be due to keto-enol tautomerism in the β -diketones. The refractive indices in Tables 1 and 2 have therefore been measured 2–3 days after the final distillation, when the keto-enol equilibrium was supposed to have been reached. Rather abnormal values were otherwise obtained, as the keto and enol forms respectively will have different refractive indices.

The infrared spectra of the alkylated acetylacetones showed a strong absorption

¹ Part XV. Lawesson, S.-O., Andersson, M., and Berghlund, C., *Arkiv Kemi* 17, 429 (1961).

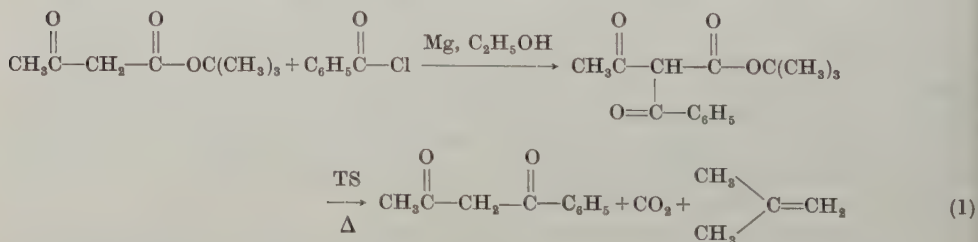
² On leave of absence from Department of Chemistry, Institute of Technology, Helsinki, Finland.

$$\begin{array}{c} \text{O} \quad \text{R} \quad \text{O} \\ \parallel \quad | \quad \parallel \\ \text{CH}_3-\text{C}-\text{CH}-\text{C}-\text{CH}_3 \end{array}$$
 Table 1. The preparation of acetylacetones:

R	Reaction time (hr)	Yield %	B.p. °C	mmHg	n_D^{20}	Reported constants			Ref.
						Yield %	B.p. °C	mm Hg	
C ₂ H ₅	18	75	179–184	760	1.4387	52	175–178	740	12
<i>i</i> -C ₃ H ₇	120	19	71–72	13	1.4346	35	180–183	740	12
allyl	4	65	75–82	10	1.4683	78	195–196	760	13
<i>n</i> -C ₄ H ₉	64	73	101–104	17	1.4443	38	90–94	10	12
<i>i</i> -C ₅ H ₁₁	40	29	98–104	10	1.4454	—	220–225	760	14
C ₆ H ₅ —CH ₂	66	64	146–153	13	1.5281	48	155–160	5	12

at 1700 cm⁻¹ and the corresponding benzoyl acetones showed one CO-bond at 1720 cm⁻¹ and another in the range of 1690–1675 cm⁻¹. As both acetylacetone and benzoylacetone absorb around 1600 cm⁻¹, there seems to be a difference between substituted and unsubstituted β -diketones which presumably might be explained by the different tendency to enolization.

From Tables 1 and 2 it is seen that most of the alkylated products have been obtained in high yields, often higher than those in the literature. Only alkylation with secondary halides gave low yields in spite of extension of the reaction time. We have also tried to use another method for the preparation of substituted β -diketones. According to Treibs and Hintermeier [15], a new method of preparing benzoylacetone is to benzoylate the alkoxy-magnesium derivative of *t*-butyl acetoacetate and then eliminate the carbo-*t*-butoxy group:



Instead of using Lund's method, we modified the syntheses and prepared the sodium compound from *t*-butyl acetoacetate and sodium hydride, which was then reacted with benzoyl chloride; the yield of benzoylacetone was found to be 68%. However, when alkylated *t*-butyl acetoacetate was allowed to react similarly, only low yields of β -diketones were isolated, presumably due to both C- and O-benzoylation.

The preparation of the sodium compounds of the β -diketones were easily made from sodium hydride in benzene, often with heating. The sodium compounds were in most cases insoluble in benzene and precipitated. The reaction of the sodium compound with benzoyl peroxide occurred at about 0°C and an excess of sodium compound was generally used so that all peroxide was consumed. In a few cases, there was

Table 2. The preparation of benzoylacetones: $\text{CH}_3-\overset{\text{O}}{\parallel}\text{C}-\overset{\text{R}}{\text{CH}}-\overset{\text{O}}{\parallel}\text{C}-\text{C}_6\text{H}_5$

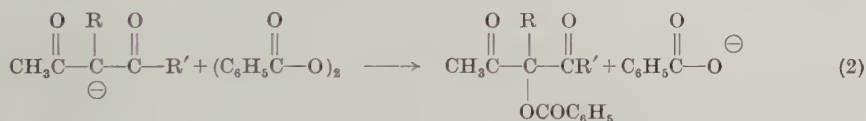
R	Reaction time (hr)	Yield %	B.p. °C	mm Hg	n_D^{20}
CH_3^a	6	94	138–142	12	1.5370
allyl	15	90	149–154	10	1.5386
$n\text{-C}_4\text{H}_9$	42	77	163–169	12	1.5188
$\text{sec-C}_4\text{H}_9$	158	31	157–161	12	1.5235
$i\text{-C}_5\text{H}_{11}$	40	62	96–102	0.1	1.5145
$\text{C}_6\text{H}_5\text{CH}_2^b$	42	68	55–56 ^c	—	—

^a Prepared in 88 % yield [11], b.p. 130–134°C/mm Hg.

^b Prepared in 47 % yield [12], m.p. 55–56°C and in 50 % yield [16], m.p. 60–61°C.

^c m.p.

unconsumed benzoyl peroxide remaining which, however, is destroyed by shaking the solution with sodium iodide in glacial acetic acid. The stoichiometry of the reaction is as follows:



From Tables 3 and 4, it is seen that derivatives of acetylacetone have in general given higher yields of benzoates than those of benzoylacetone. This was presumably due to some decomposition of the latter compounds during the final distillation; it

Table 3. Preparation of benzoyloxy-acetylacetones: $\text{CH}_3-\overset{\text{O}}{\parallel}\text{C}-\overset{\text{R}}{\underset{\text{OCOC}_6\text{H}_5}{\text{CH}}}-\overset{\text{O}}{\parallel}\text{C}-\text{CH}_3$

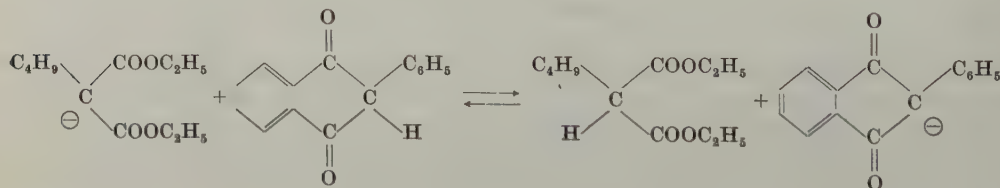
R	Yield, %	B.p. (°C)	mm Hg	M.p. (°C)	n_D^{20}
H	41	115–119	0.3		1.5241
$\text{C}_6\text{H}_5\text{CO}_2$	35	—	—	142–143	—
C_2H_5	82	132–136	0.5	—	1.5129
$i\text{-C}_3\text{H}_7$	27	124–126	0.2	—	1.5139
allyl	90	142–145	0.6	—	1.5187
$n\text{-C}_4\text{H}_9$	89	135–139	0.3	—	1.5075
$i\text{-C}_5\text{H}_{11}$	86	128–132	0.1	—	1.5027
$\text{C}_6\text{H}_5\text{CH}_2$	76	—	—	71.5–72.5	—

Table 4. The preparation of benzoyloxy-benzoylacetones: $\text{CH}_3-\overset{\text{O}}{\overset{\parallel}{\text{C}}}-\overset{\text{R}}{\underset{\text{OCOC}_6\text{H}_5}{\text{C}}}-\overset{\text{O}}{\overset{\parallel}{\text{C}}}-\text{C}_6\text{H}_5$

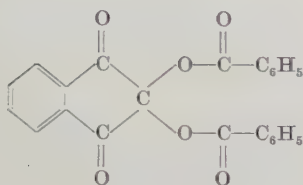
R	Yield, %	B.p. (°C)	mm Hg	M.p. (°C)	n_D^{20}
H	55	152-157	0.3	—	1.5800
C ₆ H ₅ CO ₂	11	—	—	118.5-119.5	—
CH ₃	78	—	—	100.5-101.5	—
allyl	72	163-165	0.15	—	1.5677
<i>n</i> -C ₄ H ₉	61	170-172	0.2	—	1.5535
<i>sec</i> -C ₄ H ₉	15	171-175	0.2	—	1.5580
<i>i</i> -C ₃ H ₇	55	175-180	0.1	—	1.5486
C ₆ H ₅ CH ₂	83	—	—	126.5-127.5	—

was further observed that 3-*i*-propyl acetylacetone and 3-*sec*-butyl benzoylacetone gave low yields of the benzoate (the sodium hydride reacted very slowly in these cases and the benzoyl peroxide was not completely consumed).

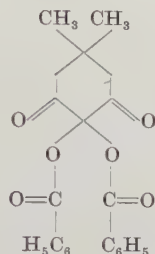
It was originally planned to investigate a series of cyclic β -diketones but difficulties were encountered that imposed certain limitations. It was found, for instance, that sodium hydride in benzene did not react with either indandione, 2-phenylindandione or 5,5-dimethyl-1,3-cyclohexanedione. The sodium hydride used apparently became inactivated or perhaps covered with the first-formed sodium derivative of the respective β -carbonyl compound. The problem was thus to find a way to introduce the sodium; it was only possible to use inert solvents, alcoholic solutions not being permissible as the alkoxide ion attacks the peroxide at the carbonyl group faster than the sodium compound of the β -carbonyl compound can rupture the oxygen-oxygen bond. Eventually it was found that if some kind of an entrainer technique was used the sodium could be introduced into the β -carbonyl compound. The reaction with benzoyl peroxide resulted in the desired benzoate, although in low yields. The method we used was to prepare the sodium compound of diethyl *n*-butyl malonate in benzene by the usual procedure. This sodium compound was soluble in benzene and when one of the slow-reacting β -carbonyl compounds was added, a thick porridge-like benzene-insoluble precipitate resulted, indicating that a new compound had been found. After reacting with benzoyl peroxide, the diethyl *n*-butyl malonate was always recovered and no tartronate isolated. This method, which appears to be without precedent, is possible due to the fact that diethyl *n*-butyl malonate is thought to be less acidic than the corresponding β -carbonyl compounds. The equilibrium would thus be to the right in the following equilibrium:



With indandione and 5,5-dimethyl-1,3-cyclohexanedione only the dibenzoyloxy compounds were isolated.

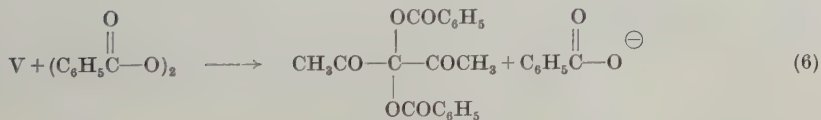
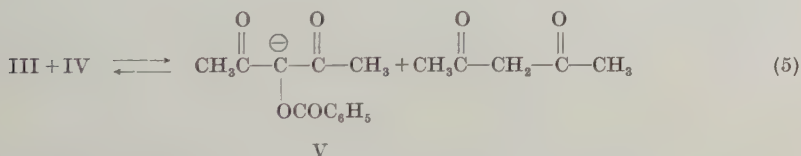
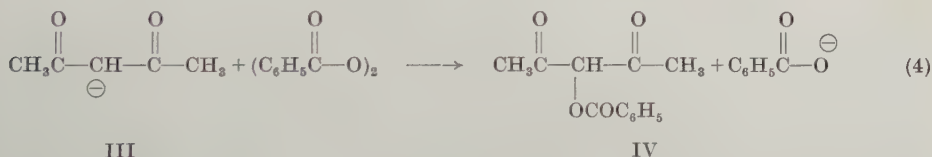


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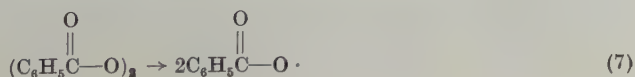


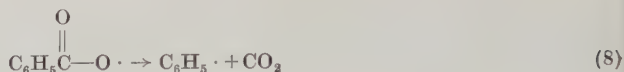
II

In the case of acetylacetone and benzoylacetone, a mixture of the mono- and disubstituted derivatives were isolated. As the monobenzoyloxy derivative of, for instance, acetylacetone has a more acidic nature than the starting material, the following reactions could explain the formation of the products:



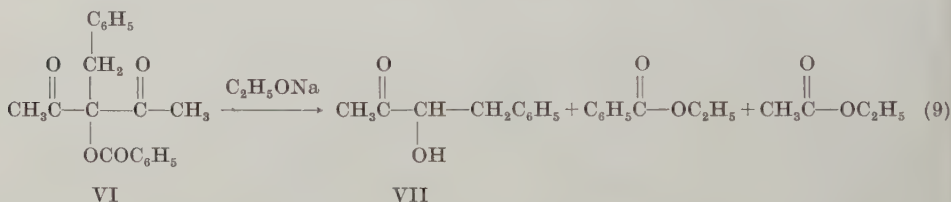
The above scheme does not say anything about the mechanism of the reaction between benzoyl peroxide and the sodium derivatives of the so-called active methylene compounds; they only give the stoichiometry of the reaction. As gas is not generated, and in almost all cases quantitative yields of benzoic acid are isolated, a conventional free-radical mechanism is excluded as this would mean that benzoyl peroxide, to some extent, would be ruptured according to the following [17]:





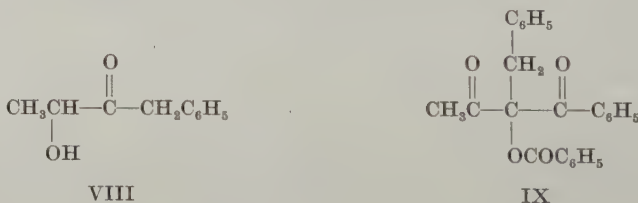
We prefer instead the working hypothesis that a perester is some kind of cyclic intermediate, which then rearranges to the final benzoate, or that a carbanion attacks the oxygen-oxygen bond directly [2]. A more thorough discussion of this will be postponed until the study of the reaction between benzoyl peroxide (carbonyl O^{18}) and malonates has been completed [18].

In order to characterize the new compounds and also to explore the synthetic utilities of the prepared benzoyloxy compounds, a few ethanolysis experiments were made. As ethanolysis of β -diketones might give mixtures of fragments, we investigated only the derivatives VI and IX, which both gave fragments which were easy to separate from each other. When VI was treated with sodium ethoxide in ethanol, it was possible to isolate ethyl benzoate and 1-phenyl-2-ol-3-one-butane:



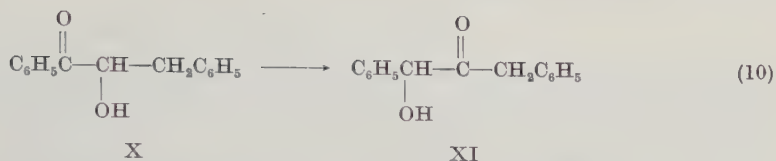
The formed ethyl acetate, distilled into the solvent, was not isolated. It is, however, clear that the ethoxide ion attacks both the benzoyl and acetyl groups.

The acyloin, VII, is not described in the literature but the O-benzoyl derivative has recently been prepared [6]. By hydrolyzing it with a base, a compound was ob-

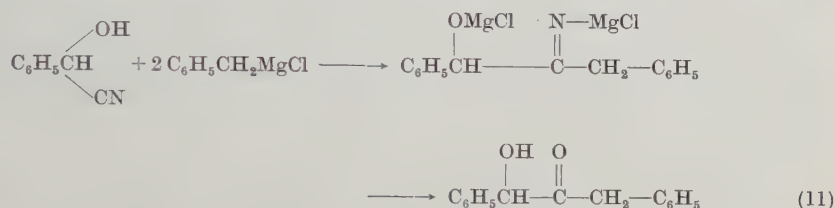


tained identical to VII by infrared and VPC analyses. To ascertain that VII had not isomerized to VIII, the latter was prepared by a general method [19] from lactonitrile and benzylmagnesium chloride; VII and VIII definitely had not the same retention time and seem not to be identical compounds. A similar investigation [6] shows that acyloins in question do not isomerize.

Ethanolysis of IX gave ethyl benzoate, small amounts of 1-phenyl-2-ol-3-one-butane and a solid with m.p. 115–116°C. From IR it was seen that the solid contained hydroxy and carbonyl groups. Analysis gave $\text{C}_{15}\text{H}_{14}\text{O}_2$, which made us believe that 1,3-diphenyl-1-one-2-ol-propane, X, had been found. However, the last compound had been prepared earlier [20] and had the m.p. 65–66°C, so isomerization had apparently occurred according to the following:



1,3-diphenyl-1-ol-2-one-propane (XI) was also prepared according to the following:



and shown to be identical with the ethanolysis product.

Experimental

The reactions between benzoyl peroxide and the sodium compound of β -diketones were performed in an atmosphere from which moisture was rigidly excluded. Benzoyl peroxide was recrystallized from methanol and chloroform at low temperatures. Experiments with Grignard reagents were run in a nitrogen atmosphere. The sodium hydride (Kebo) was the ordinary laboratory reagent. The infrared spectra were recorded on a Perkin-Elmer Model 137 (Infracord). The analyses were made by Dr. Alfred Bernhardt, Mülheim (Ruhr), and the Analytical Department of Uppsala University. Boiling and melting points are uncorrected.

Alkylation of acetylacetone

The same general procedure was used in all cases; the preparation of 3-*n*-butyl-acetylacetone is given as an example. Allyl bromide and benzyl chloride were used; in all other cases iodides were needed.

3-*n*-Butyl-acetylacetone

30 g (0.3 mole) of acetylacetone, dissolved in 100 ml of ether, were added to 7.2 g (0.3 mole) of sodium hydride, covered with 100 ml of ether. The sodium compound soon precipitated and after stirring for 1 hour, the ether was stripped off: 300 ml of dry, redistilled dioxane were added and the mixture heated to reflux. 83 g (0.45 mole) of *n*-butyl iodide were added dropwise for 30 minutes and gentle reflux was then maintained for 64 hours. The dioxane was distilled off and water added. The water solution was extracted with ether and the combined extracts were washed with water, dried over sodium sulphate, concentrated, and distilled. B.p. 101–104°C/17 mm Hg, $n_D^{20} = 1.4443$. Yield 34.1 g (73 %).

Alkylation of benzoylacetone

The general procedure was the same in all cases and some examples are given. Allyl bromide and benzyl chloride were used; in all other cases iodides were needed.

3-Allyl-benzoylacetone

32.4 g (0.2 mole) of benzoylacetone in 200 ml of dry ether were added with stirring and cooling to 4.8 g (0.2 mole) of sodium hydride, covered with 75 ml of ether. The sodium compound was obtained as a yellow precipitate. The mixture was stirred for one hour at room temperature, and the ether then stripped off; 200 ml of dioxane were added and heat was applied till gentle reflux, after which 36.6 g (0.3 mole) of allyl bromide were added dropwise for 30 minutes and reflux maintained for 15 hours. The work-up was performed in the usual way. The main fraction had a b.p. 149–154°C/10 mm Hg, $n_D^{20} = 1.5386$. Yield 36.3 g (90%). The product was a colourless liquid which gave a violet enol-test with FeCl_3 .

Anal. $\text{C}_{13}\text{H}_{14}\text{O}_2$

Calc. C 77.20, H 6.98

Found C 77.19, H 7.08

3-sec-Butyl-benzoylacetone

0.2 mole of the sodium compound and 59 g (0.32 mole) of sec-butyl iodide were refluxed in 200 ml of dioxane for 158 hours, after which time the reaction mixture was still not neutral. The work-up was made in the usual way and a crude product (18.6 g) was obtained with b.p. 149–163°C/11 mm Hg. From this, benzoyl acetone was extracted with 1% sodium hydroxide solution. From the purified crop, 13.7 g (31%) of the named product were isolated as a colourless liquid giving a negative enol-test.

Anal. $\text{C}_{14}\text{H}_{18}\text{O}_2$:

Calc. C 77.03, H 8.31

Found C 76.98, H 8.30

3-iso-Amyl-benzoylacetone

0.2 mole of the sodium compound of benzoylacetone, and 63.5 g (0.32 mole) of iso-amyl iodide in 200 ml of dioxane were refluxed for 40 hours. Yield 28.9 g (62%) of a colourless liquid (b.p. 96–102°C/0.1 mm Hg, $n_D^{20} = 1.5145$), which gave a violet enol-test.

Anal. $\text{C}_{15}\text{H}_{20}\text{O}_2$:

Calc. C 77.55, H 8.68

Found C 77.55, H 8.70

3-Benzyl-benzoylacetone

0.6 mole of the sodium compound of benzoylacetone and 114 g (0.9 mole) of benzyl chloride in 600 ml of dioxane were refluxed for 42 hours. The crude product, b.p. 155–170°C/0.4 mm Hg, weighed 119 g and had the m.p. 48–50°C. Recrystallization from ether and pet. ether gave 103 g (68%) of white needles with m.p. 55–56°C. The enol-test of the compound in alcohol was negative. In the literature, different melting points are reported [12, 16].

Anal. $\text{C}_{17}\text{H}_{18}\text{O}_2$:

Calc. C 80.92, H 6.39

Found C 81.18, H 6.45

The preparation of benzoylacetone from t-butyl acetoacetate

23.7 g (0.15 mole) of *t*-butyl acetoacetate were added with stirring to 3.6 g (0.15 mole) of sodium hydride covered with 200 ml of dry benzene. A gray-white precipitate of the sodium compound was formed. After all hydride had been consumed, 21.1 g (0.15 mole) of benzoyl chloride were added and the mixture refluxed for 10 minutes. The mixture was poured into water, the benzene separated and the water-phase twice extracted with ether. The combined organic layers were washed until neutral with water, dried over sodium sulphate and the solvents stripped off. 0.3 g of *p*-toluene sulphonic acid was added and, when warmed on an oil bath (150°C), gas-evolution started. When the system had reached constant pressure again (the flask was connected to a water-pump) distillation was made and the main fraction obtained with b.p. 131–134°C/10 mm Hg. Yield 16.6 g (68 %). Recrystallization from pet. ether gave m.p. 54.5–55.5°C.

The preparation of 3-n-butyl benzoylacetone from t-butyl n-butyl acetoacetate

32.1 g (0.15 mole) of *t*-butyl *n*-butylacetoacetate were added with stirring to 3.6 g (0.15 mole) of sodium hydride covered with 250 ml of dry benzene. Heat was applied for 30 minutes so that all hydride was consumed. 21.1 g (0.15 mole) of benzoyl chloride was added to the sodium derivation at room temperature and the mixture then refluxed for 10 minutes. The mixture was poured into water, the benzene separated and the water layer extracted with ether. The combined organic layers were washed with water until neutral and dried over sodium sulphate. The work-up and decomposition (150°C) of the ester were made as above. Distillation gave a crude product, b.p. 105–183°C/11 mm Hg, which was acidic. Ether was added and after washing with sodium bicarbonate and water, a repeated distillation gave 3-*n*-butylbenzoylacetone, b.p. 166–174°C/15 mm Hg, $n_D^{20} = 1.5175$. Yield 11.5 g (35 %). Identification was made by IR and VPC with authentic *n*-butyl benzoylacetone.

The preparation of benzoyloxy- and dibenzoyloxy-acetylacetone

20 g (0.20 mole) of acetylacetone were added with stirring to 4.8 g (0.2 mole) of sodium hydride covered with 200 ml of dry benzene. All hydride was consumed after heating for one hour. The mixture was cooled in an ice-bath and 36.3 g (0.15 mole) of benzoyl peroxide in 300 ml of dry benzene added during 45 minutes. After stirring overnight, the peroxide test was negative. The mixture was poured into water, the benzene separated and the water phase extracted with ether. The organic layers were combined, washed until neutral with water and dried over sodium sulphate. (From the water phase 19.4 g of benzoic acid were isolated.) The solvents were stripped off, the excess of acetylacetone distilled off at water-pump pressure and from the residue a main fraction was obtained with b.p. 115–119°C/0.3 mm Hg, $n_D^{20} = 1.5241$. Yield 13.5 g (41 %). The product, 3-benzoyloxyacetylacetone, was a viscous faintly yellow liquid, which gave a violet enol-test.

Anal. $C_{12}H_{12}O_4$:

Calc.	C 65.44,	H 5.49
Found	C 65.11,	H 5.42

The residue solidified after cooling and recrystallization from ethanol gave white crystals, m.p. 142–143°C. Yield 8.8 g (35 %).

Anal. $C_{19}H_{16}O_6$:

Calc.	C 67.05,	H 4.75
Found	C 66.71,	H 4.58

3-Ethyl-3-benzoyloxy-acetylacetone

The benzene-soluble sodium compounds was prepared from 12.8 g (0.1 mole) of 3-ethyl-acetylacetone and 2.4 g (0.1 mole) of sodium hydride in 200 ml of benzene. After cooling to zero, 18.2 g (0.075 mole) of benzoyl peroxide in 200 ml of benzene were added for 30 minutes. After stirring overnight (peroxide test: neg.) the work-up was made as above. Isolated benzoic acid: 9 g. The main fraction had b.p. 132–136°C/0.5 mm Hg, $n_D^{20} = 1.5129$. Yield 15.2 g (83 %). The product was a faintly yellow and viscous liquid.

Anal. $C_{14}H_{16}O_4$:

Calc.	C 67.73,	H 6.50
Found	C 67.79,	H 6.59

3-*i*-Propyl-3-benzoyloxy-acetylacetone

The benzene-soluble sodium derivative was slowly prepared from 7.1 g (0.05 mole) of 3-*i*-propylacetylacetone and 1.2 g (0.05 mole) of sodium hydride in 100 ml of benzene with heating for 8 hours. 9.7 g (0.04 mole) of benzoyl peroxide in 100 ml of benzene was added to the cooled solution and stirred overnight, after which the peroxide-test was positive. The mixture was worked up as usual; 3.7 g of benzoic acid were isolated. Distillation gave the benzoate with b.p. 124–126°C/0.2 mm Hg, $n_D^{20} = 1.5139$. Yield 3.5 g (27 %) as a viscous, green-yellow liquid.

Anal. $C_{15}H_{18}O_4$:

Calc.	C 68.68,	H 6.92
Found	C 68.76,	H 6.93

3-Allyl-3-benzoyloxy-acetylacetone

The insoluble sodium compound was prepared from 19.6 g (0.14 mole) of 3-allyl-acetylacetone and 3.36 g (0.14 mole) of sodium hydride in 200 ml of benzene. Reaction with 24.2 g (0.1 mole) of benzoyl peroxide in 200 ml of benzene was made as above. The peroxide test was negative after 2 hours. 12 g of benzoic acid were isolated. The benzoate had b.p. 142–145°C/0.6 mm Hg, $n_D^{20} = 1.5187$. Yield 23.4 g (90 %) and was a colourless and viscous liquid.

Anal. $C_{15}H_{16}O_4$:

Calc.	C 69.21,	H 6.20
Found	C 69.06,	H 6.22

3-*n*-Butyl-3-benzoyloxy-acetylacetone

The benzene-soluble sodium compound of 3-*n*-butyl-acetylacetone was prepared from 3.36 g (0.14 mole) of sodium hydride and 21.8 g (0.14 mole) of the ester in 200 ml of benzene. Reaction with 24.2 g (0.1 mole) of benzoyl peroxide in 200 ml of benzene was made as above and, after 1–2 hours, the peroxide test was negative. The work-up gave 11.7 g of benzoic acid and the benzoate, b.p. 135–139°C/0.3 mm Hg, $n_D^{20} = 1.5075$, yield 24.6 g (89 %) as a viscous and colourless liquid.

Anal. $C_{16}H_{20}O_4$:

Calc.	C 69.54,	H 7.30
Found	C 69.52,	H 7.30

3-i-Amyl-3-benzoyloxy-acetylacetone

11.9 g (0.07 mole) of 3-*i*-amylacetylacetone were added to 1.7 g (0.07 mole) of sodium hydride, covered with 100 ml of dry benzene. The reaction was slow, but after heating for some time, a clear solution of the sodium compound was formed. Reaction with 12.1 g (0.05 mole) of benzoyl peroxide in 100 ml of benzene as above; the peroxide test was negative after 2 hours. The work-up gave 5.8 g of benzoic acid and the benzoate, b.p. 128–132°C/0.1 mm Hg, $n_D^{20} = 1.5027$. Yield 12.5 g (86 %) as a faintly yellow and viscous liquid.

Anal. $C_{17}H_{22}O_4$:

Calc. C 70.32, H 7.64

Found C 70.65, H 7.74

3-Benzyl-3-benzoyloxy-acetylacetone

95 g (0.5 mole) of 3-benzyl-acetylacetone were reacted with 12.0 g (0.5 mole) of sodium hydride in 700 ml of dry benzene. Heating for an hour drove the reaction to completion and a white precipitate was formed. After cooling to 0°C, 89.5 g (0.37 mole) of benzoyl peroxide in 750 ml of dry benzene were added for 2 hours. Stirring overnight gave a negative peroxide test. The work-up gave 44 g of benzoic acid and, after solvents and excess starting material had been distilled off, a yellow oil remained. After addition of pet. ether the oil solidified and recrystallization from benzene – pet. ether gave white needles, m.p. 71.5–72.5°C. Yield 87 g (76 %).

Anal. $C_{19}H_{18}O_4$:

Calc. C 73.53, H 5.85

Found C 73.59, H 5.86

The preparation of benzoyloxy- and dibenzoyloxy-benzoylacetone

16.2 g (0.1 mole) of benzoylacetone, dissolved in 100 ml of dry benzene, were added with stirring to 2.4 g (0.1 mole) of sodium hydride covered with 200 ml of dry benzene. The sodium compound was insoluble in benzene. The mixture was cooled in an ice-water bath to 0°C and 18.2 g (0.075 mole) of benzoyl peroxide in 150 ml of benzene were added dropwise for 30 minutes. After stirring overnight, the test for peroxides was negative. The usual work-up gave 9.2 g of benzoic acid. From the organic phase, the solvents were stripped off and the excess of benzoylacetone was distilled off at 0.1 mm Hg. The remainder was dissolved in ethanol and placed in a refrigerator; after some time, white crystals precipitated, and were filtered off and recrystallized from ethanol. M.p. 118.5–119.5. Yield 1.7 g (11 %).

Anal. $C_{24}H_{18}O_6$:

Calc. C 71.63, H 4.51

Found C 71.68, H 4.52

The alcohol was stripped off from the alcohol solution, ether was added and, after washing once with water, the ether layer was dried over sodium sulphate. Distillation gave the monobenzoate, b.p. 152–157°C/0.3 mm Hg, $n_D^{20} = 1.5800$. Yield 11.7 g (55 %) as a faintly yellow and viscous liquid.

Anal. $C_{17}H_{14}O_4$:

Calc. C 72.33, H 5.00

Found C 72.34, H 5.02

3-Methyl-3-benzoyloxy-benzoylacetone

The sodium compound was prepared from 3.36 g (0.14 mole) of sodium hydride and 24.4 g (0.14 mole) of 3-methyl-benzoylacetone in 200 ml of benzene; it was then reacted with 24.2 g (0.1 mole) of benzoyl peroxide in 200 ml of benzene in the usual way. After stirring overnight, the work-up was made as above. 11.8 g of benzoic acid were isolated. The benzoate was found to be a solid, which gave white needles (from benzene + pet.ether) with m.p. 100.5–101.5°C. Yield 23.1 g (78 %).

Anal. $C_{18}H_{16}O_4$:

Calc. C 72.96, H 5.44
Found C 72.91, H 5.45

3-Allyl-3-benzoyloxy-benzoylacetone

28.3 g (0.14 mole) of 3-allyl-benzoylacetone were reacted with 3.36 g (0.14 mole) of sodium hydride in 200 ml of dry benzene and, to the final insoluble sodium compound, 24.2 g (0.1 mole) of benzoyl peroxide in 200 ml of benzene were added for 30 minutes. The mixture was worked up in the usual way and gave 12.7 g of benzoic acid and the benzoyloxy derivative with b.p. 163–165°C/0.15 mm Hg, $n_D^{20} = 1.5677$. Yield 23.5 g (73 %). The product was a very viscous liquid.

Anal. $C_{20}H_{18}O_4$:

Calc. C 74.52, H 5.63
Found C 74.47, H 5.62

3-n-Butyl-3-benzoyloxy-benzoylacetone

28.4 g (0.13 mole) of 3-n-butyl benzoylacetone were added to 3.1 g (0.13 mole) of sodium hydride in 150 ml of benzene and the soluble sodium compound was then allowed to react with 24.2 g (0.1 mole) of benzoyl peroxide in the usual way. The work-up gave 12.6 g of benzoic acid and the benzoyloxy compound had b.p. 170–172°C/0.2 mm Hg, $n_D^{20} = 1.5535$. Yield 20.7 g (61 %).

Anal. $C_{21}H_{22}O_4$:

Calc. C 74.53, H 6.55
Found C 74.46, H 6.54

3-sec-Butyl-3-benzoyloxy-benzoylacetone

After gently heating together for 10 hours 12.2 g (0.056 mole) of 3-sec-butyl benzoylacetone and 1.45 g (0.06 mole) of sodium hydride in 100 ml of benzene, almost all the hydride had been consumed and a precipitate formed. 9.7 g (0.04 mole) of benzoyl peroxide in 100 ml of benzene were added to the mixture at 0°C and stirring was continued overnight. A positive peroxide test was noted. The normal work-up gave 4.7 g of benzoic acid and 4.2 g of a crude acidic fraction, b.p. 135–190°C/0.2 mm Hg. Ether was added to this fraction and repeated extractions with sodium bicarbonate and water was made. Distillation of the dried organic phase gave a fraction with b.p. 171–175°C/0.2 mm Hg, $n_D^{20} = 1.5580$. Yield 2 g (15 %).

Anal. $C_{21}H_{22}O_4$:

Calc. C 74.53, H 6.55
Found C 74.68, H 6.80

3-i-Amyl-3-benzoyloxy-benzoylacetone

The sodium compound was prepared from 23.2 g (0.1 mole) of 3-i-amyl-benzoylacetone and 2.4 g (0.1 mole) of sodium hydride in 250 ml of benzene. 18.2 g (0.075 mole)

of benzoyl peroxide in 150 ml of benzene were added to the clear solution kept at 0°C. The usual work-up gave 8.9 g of benzoic acid and the main fraction with b.p. 175–180°C/0.1 mm Hg, $n_D^{20} = 1.5486$. Yield 14.6 g (55 %).

Anal. $C_{22}H_{24}O_4$:

Calc. C 74.97, H 6.86

Found C 74.76, H 6.86

3-Benzyl-3-benzoyloxy-benzoylacetone

101 g (0.4 mole) of 3-benzylbenzoylacetone in 400 ml of benzene were added to 9.6 g (0.4 mole) of sodium hydride in 200 ml of benzene. The sodium compound formed a white precipitate and further reaction with 72.6 g (0.3 mole) of benzoyl peroxide in 600 ml of benzene was carried out as above. The usual work-up gave 38 g of benzoic acid and a solid with m.p. 126–127.5°C. Yield 92.5 g (83 %). Recrystallization from ethanol gave white prisms with m.p. 126.5–127.5°C.

Anal. $C_{24}H_{20}O_4$:

Calc. C 77.40, H 5.41

Found C 77.56, H 5.42

The preparation of 2,2-dibenzoyloxy-5,5-dimethyl-1,3-cyclohexanedione

The sodium compound of diethyl *n*-butyl malonate was prepared from 2.4 g (0.1 mole) of sodium hydride and 21.6 (0.1 mole) of the malonate in 200 ml of benzene. 14 g (0.1 mole) of dimedone were added and, after stirring, the mixture was cooled to 0°C and 18 g (0.075 mole) of benzoyl peroxide in 200 ml of benzene were added. After stirring for 9 hours, tests for peroxides were still positive. Following the usual work-up, 17 g of diethyl *n*-butyl malonate (b.p. 83°C/3 mm Hg, $n_D^{20} = 1.4248$) were recovered and 2.1 g of a solid, which after recrystallization from ether + pet. ether, gave small, white needles with the m.p. 149.5–151°C.

Anal. $C_{23}H_{14}O_6$:

Calc. C 71.50, H 3.68

Found C 71.30, H 3.88

Mol.wt. calc. 386, found 392.

The preparation of 2,2-dibenzoyloxy-indandione

21.6 g (0.1 mole) of diethyl *n*-butylmalonate and 2.4 g (0.1 mole) of sodium hydride in 160 ml of benzene gave the corresponding sodium compound; 11.5 g (0.08 mole) of indandione were added and, after stirring for one hour, the mixture was cooled and 17 g (0.7 mole) of benzoyl peroxide in 200 ml of benzene were added. The mixture was stirred for 15 hours and worked up as above. 9 g of benzoic acid were isolated and, from the neutral phase, a solid was formed (3.4 g) which after recrystallization from ethanol gave glistering needles with m.p. 194–195°C.

Anal. $C_{23}H_{20}O_6$:

Calc. C 69.46, H 5.30

Found C 69.04, H 5.43

Mol.wt. calc. 380, found 365.

2-Phenyl-2-benzoyloxy-indandione

21.6 g (0.1 mole) of diethyl *n*-butyl malonate and 2.4 g (0.1 mole) of sodium hydride in 260 ml of benzene gave the sodium compound, (0.1 mole) of 2-phenylindandione were added and, after stirring for 45 minutes, 18 g (0.075 mole) of benzoyl peroxide

in 200 ml of benzene were added dropwise to the cooled solution. The mixture was stirred for 15 hours and then worked up as above. 16 g of diethyl *n*-butyl malonate were recovered, 12.5 g of crude benzoic acid (+ 2-phenylindandione) and 25 g of a neutral solid product. Continuous extraction of the latter gave a small amount of the benzoyloxy compound consisting of white crystals (from ethanol) with m.p. 119.5–121°C.

Anal. C₂₂H₁₄O₄:

Calc. C 77.18, H 4.12

Found C 77.27, H 4.28

Mol.wt. calc. 342, found 331.

Alcoholysis of 3-benzyl-3-benzoyloxy-acetylacetone

The sodium alcoholate was prepared from 2.3 g (0.1 mole) of sodium and 50 ml of absolute alcohol, which was added dropwise at room temperature to 31.0 g (0.1 mole) of benzyl benzoyloxy-acetylacetone in 50 ml of ethylalcohol. Stirring was maintained for 22 hours and the mixture was then poured into water. The water layer was extracted with ether 2–3 times and the combined extracts washed until neutral and dried over sodium sulphate. Distillation gave 10.8 g (72 %) of ethylbenzoate, b.p. 86–90°C/11 mm Hg, $n_D^{20} = 1.5064$ and 2.3 g (14 %) of a product identified as 4-phenylbutane-2-one-3-ol, b.p. 129–134°C/10 mm Hg, $n_D^{20} = 1.5291$.

Anal. C₁₀H₁₂O₂:

Calc. C 73.14, H 7.37

Found C 72.56, H 7.43

When the water layer was acidified benzoic acid precipitated and a continuous extraction of the water phase gave 1.6 g of benzoic acid.

Preparation of 1-phenyl-2-ol-3-one-butane

10.7 g (0.04 mole) of 1-phenyl-2-benzoyloxy-3-one-butane were heated with 200 ml of 10 % sodium hydroxide solution for 60 minutes at 60°C. The water phase was extracted with ether, the combined extracts washed until neutral and dried over sodium sulphate. Distillation gave the acyloin with the b.p. 128–131°C/10 mm Hg, $n_D^{20} = 1.5293$. Yield 1.2 g (18 %).

Anal. C₁₀H₁₂O₂:

Calc. C 73.14, H 7.37

Found C 73.13, H 7.37

Preparation of 1-phenyl-2-one-3-ol-butane

Benzylmagnesium chloride was prepared from 12 g of magnesium in 225 ml of ether and 51 g (0.4 mole) of benzyl chloride. 14.2 g (0.2 mole) of lactonitrile in 50 ml of ether were then added dropwise for 75 minutes; the ether refluxed gently due to the exothermic reaction and was then refluxed for 2 hours. After cooling, the mixture was poured into water + hydrochloric acid and the water layer extracted three times with ether. After the usual work-up, distillation gave the main fraction with the b.p. 145°C/15 mm Hg, $n_D^{20} = 1.5301$. Yield 8.1 g (25 %).

Anal. C₁₀H₁₂O₂:

Calc. C 73.14, H 7.37

Found C 73.02, H 7.46

Alcoholysis of 3-benzyl-3-benzoyloxy-benzoylacetone

The sodium alcoholate was prepared from 2.3 g (0.1 mole) of sodium and 50 ml of absolute ethanol and added with stirring to 37.2 g (0.1 mole) of benzylbenzoyloxy-benzoylacetone in 50 ml of ethanol. After 24 hours at room temperature, the mixture was poured into water and extracted with ether. The extracts were washed with water, dried and distilled; 16 g (53 %) of ethyl benzoate with b.p. 85–89°C/10 mm Hg, $n_D^{20} = 1.5063$, and 1.3 g (8 %) of 4-phenylbutane-2-one-3-ol., b.p. 138–140°C/15 mm Hg, $n_D^{20} = 1.5282$. Further distillation gave a fraction with b.p. 130–150°C/0.4 mm Hg, which solidified after some time; 1.9 g white needles was obtained with the m.p. 115–116°C. A mixed melting point with 1,3-diphenyl-1-ol-2-one-propane gave no depression.

Preparation of 1,3-diphenyl-1-ol-2-one-propane

A. *Preparation of mandelonitrile*: Mandelonitrile was prepared according to Organic Syntheses [21] from 50 g (0.1 mole) of sodium cyanide and 106 g (1 mole) of benzaldehyde. The work-up was modified as follows. The mandelonitrile was separated and the water phase extracted with 100 ml of ether. The mandelonitrile was combined with the extract and dried over sodium sulphate for 3 hours. The sodium sulphate was filtered off and the ether solution diluted with dry ether to a total volume of 250 ml. This solution was immediately used according to B.

B. *The reaction of mandelo-nitrile and benzylmagnesium chloride*: Benzylmagnesium chloride was prepared from 10.7 g (0.44 mole) of magnesium in 225 ml of dry ether and 51 g (0.4 mole) of benzylchloride. 100 ml of ether were added to the Grignard reagent and 40 ml of the mandelonitrile solution were added with stirring during 45 minutes. After the exothermic reaction ceased, the mixture was refluxed for 2 hours. The usual work-up gave a solid which, after being washed with pet. ether followed by recrystallization from water + ethylalcohol, gave 6 g of white needles with the m.p. 115–116°C.

Anal. $C_{15}H_{14}O_2$:

Calc.	C 79.62,	H 6.24
Found	C 79.65,	H 6.25

SUMMARY

By the benzoyl peroxide method, the benzoyloxy group has been introduced into a series of alkylsubstituted acetylacetones and benzoylacetones and also into some cyclic β -diketones. The method seems to be general and, in all cases where the sodium compound is easily obtained, good yields of the benzoate are found. With the investigated cyclic β -diketones, the corresponding sodium derivatives were made by an entrainer technique.

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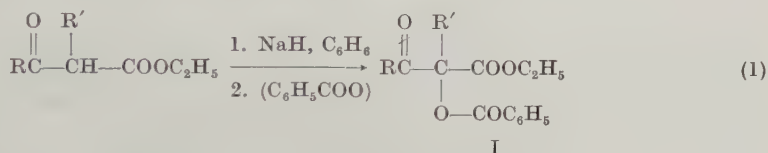
Uppsala 1961. Almqvist & Wiksells Boktryckeri AB

Studies on peroxy compounds

XVII. The preparation of acyloins from *t*-butyl acetoacetate¹

By SVEN-OLOV LAWESSON, SUSANNE GRÖNWALL and (in part)
MARGARETA ANDERSSON

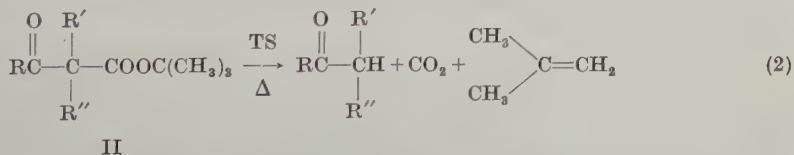
Recently Lawesson *et al.* [1] prepared α -benzoyloxy derivatives of β -ketoesters according to the peroxide method:



$\text{R} = \text{CH}_3, \text{C}_6\text{H}_5; \text{R}' = \text{alkyl or Cl}$

By alcoholysis of I, α -hydroxyesters were obtained but treatment of I with acids or bases either caused complete destruction of the ester or, when weak hydrolysis was used, the starting materials were recovered. If I had been less stable, ketone-cleavage would have given α -ketols (acyloins). Similar results were also recorded by Bradley and Robinson [2].

As in β -carbonyl compounds of type II, where $\text{R} = \text{methyl, ethoxy or } t\text{-butoxy}$ groups and R' and R'' different functional or alkyl groups, the carbo-*t*-butoxy group is easily eliminated by heating with *p*-toluenesulphonic acid (see ref. [3] for pertinent references), it should be possible to prepare acyloins starting from *t*-butyl acetoacetates.



t-Butyl acetoacetate is most easily prepared from diketene and *t*-butyl alcohol in the presence of catalytic amounts of sodium acetate [4],



¹ Part XVI. Lawesson, S.-O., Jönsson, P.-G., and Taipale, J., *Arkiv Kemi* 17, 441 (1961).

Table 1. The preparation of alkylated *t*-butyl acetoacetates:
$$\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3\text{C}-\text{CH}(\text{R})\text{COOC}(\text{CH}_3)_3 \end{array}$$

R	Reaction time (hr)	Yield %	B.p. °C	mm Hg	n_D^{20}
CH ₃	1	76	78–79	10	1.4198
C ₂ H ₅	2	68	87–88	12	1.4221
allyl	0.25	62	90	12	1.4375
<i>n</i> -C ₃ H ₇	3.5	67	93–95	12	1.4256
<i>i</i> -C ₄ H ₉	3.5	71	78–80	10	1.4270
sec-C ₄ H ₉	4.5	65	97–99	10	1.4306
<i>n</i> -C ₅ H ₁₁	2.5	67	120–22	10	1.4308
<i>i</i> -C ₅ H ₁₁	3.5	51	114	10	1.4302
<i>n</i> -C ₆ H ₁₃	1.25	63	81–82	0.4	1.4321
C ₆ H ₅ CH ₂	0.5	57	93	0.2	1.4919

and hitherto only a few derivatives have been prepared; Renfrow and Walker [5] synthesized mostly disubstituted derivatives and Treibs and Hintermeier [4] introduced different functional groups. As a continuation of our benzoyl peroxide work [1,6–10], this paper deals with a new method of preparing acyloins [11]; similar work is in progress concerning the chemistry of ethyl 3-benzoyloxy laevulinate [12] and benzoyloxy-cyclohexenones [13].

The preparation of alkyl- and aralkylsubstituted *t*-butyl acetoacetates were performed in a simpler way than that of Renfrow and Walker [5]. Thus, all alkylations were made in ethyl alcohol with sodium ethoxide as the condensation agent. No transesterification was observed and the use of *t*-butanol as solvent was found to be quite unnecessary. We severely tested this statement by alkylating *t*-butyl acetoacetate under identical conditions for 1, 2, 3 and 4 hours and, by analyzing the products by vapour phase chromatography, it was found that in no case was any derivative of ethyl acetoacetate traced but only a single product, which was the corresponding *t*-butyl acetoacetate. In this connection it was observed that the chromatograms of the β -ketoesters possessed two peaks, corresponding to the keto- and enol-forms respectively, and that derivatives of *t*-butyl acetoacetate were sensitive to heat and decomposed at high temperature.

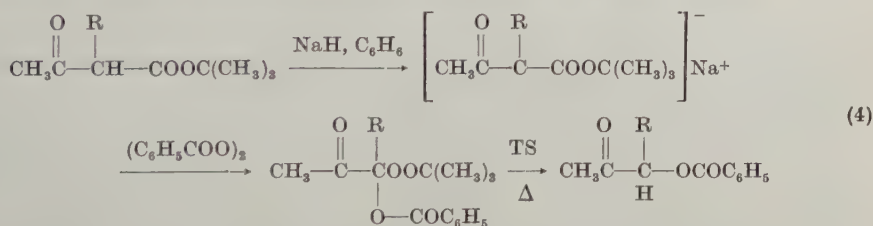
As all alkylation experiments were made according to the same procedure, only one example is given in the experimental part. From Table 1 it is seen that the reaction time is, generally speaking, rather short and that the yields are high. The benzyl derivative gave the lowest yield, which might have been due to some decomposition in the final distillation. The analytical data are recorded in Table 2 and it is observed that the carbon yield percentages are too low which may be due to incomplete combustion. It is well-known that isobutylene is easily split off from the named esters at high temperatures (see also above) which may be the cause of the unsatisfactory analyses.

The introduction of the benzoyloxy group into the *t*-butyl acetoacetates ran smoothly. Sodium hydride reacted quite normally with the ester in benzene and gentle heat was sometimes applied so that the hydride was consumed. The subsequent

Table 2. Analyses of alkylated *t*-butyl acetoacetates: $\text{CH}_3\overset{\text{O}}{\parallel}\text{C}-\text{CH}(\text{R})\text{COOC}(\text{CH}_3)_3$

R	Formula	Calc.		Found	
		C	H	C	H
CH_3	$\text{C}_9\text{H}_{16}\text{O}_3$	62.76	9.36	61.61	9.16
C_2H_5	$\text{C}_{10}\text{H}_{18}\text{O}_3$	64.49	9.74	63.73	9.65
allyl	$\text{C}_{11}\text{H}_{18}\text{O}_3$	66.64	9.15	66.62	9.14
<i>n</i> - C_3H_7	$\text{C}_{11}\text{H}_{20}\text{O}_3$	65.97	10.07	65.44	10.04
<i>i</i> - C_4H_9	$\text{C}_{12}\text{H}_{22}\text{O}_3$	67.25	10.35	66.62	10.34
sec- C_4H_9	$\text{C}_{12}\text{H}_{22}\text{O}_3$	67.25	10.35	66.62	10.34
<i>n</i> - C_5H_{11}	$\text{C}_{13}\text{H}_{24}\text{O}_3$	68.38	10.59	67.85	10.57
<i>i</i> - C_5H_{11}	$\text{C}_{13}\text{H}_{24}\text{O}_3$	68.38	10.59	67.67	10.54
<i>n</i> - C_6H_{13}	$\text{C}_{14}\text{H}_{26}\text{O}_3$	69.38	10.81	68.84	10.81
$\text{C}_6\text{H}_5-\text{CH}_2$	$\text{C}_{15}\text{H}_{20}\text{O}_3$	72.55	8.12	72.15	8.09

reaction with benzoyl peroxide was instantaneous and, after a short while, the reaction could be worked up. No gas evolution was observed in any of the performed reactions and quantitative yields of benzoic acid were isolated. Attempts to purify the α -benzoyloxy esters by distillation were unsuccessful due to extensive decomposition. However, by heating the crude products of the α -benzoyloxy compounds with catalytic amounts of *p*-toluenesulphonic acid, the carbo *t*-butoxy group was eliminated and the *O*-benzoyl derivative of the corresponding acyloins obtained



From Table 3, it is seen that high yields of the corresponding acyloin derivatives are found except in one case. With unsubstituted ester (*t*-butyl acetoacetate), decomposition occurred under the final distillation which reduced the total yield of the final, pure product. When excess of the sodium compound was used, a slightly increased yield was found. Any *O*-benzoyl acyloin derived from *t*-butyl sec-butyl acetoacetate could not be isolated. Although the reaction with benzoyl peroxide ran smoothly and quantitative yields of benzoic acid were isolated, the treatment with *p*-toluenesulphonic acid apparently caused elimination of benzoic acid. Other anomalies have also been observed with *t*-butyl acetoacetates substituted in the 2-position with sec-alkyl groups and these problems are being studied.

Hydrolysis of the *O*-benzoyl acyloins in dilute sodium hydroxide solution produced the corresponding acyloin smoothly. Only a few hydrolyses were performed and VPC analyses were made on the low-boiling acyloins. A single peak was found which indicated that no isomerization had occurred. In two cases, the corresponding iso-

$$\begin{array}{c} \text{O} \quad \text{R} \\ \parallel \quad | \\ \text{CH}_3\text{C}-\text{CH}-\text{OCOC}_6\text{H}_5 \end{array}$$

Table 3. The preparation of *O*-benzoyl acyloins: $\text{CH}_3\text{C}-\text{CH}-\text{OCOC}_6\text{H}_5$

R	Yield	(B.p. °C)	mm Hg	n_D^{20}
H ^a	38	145–146	10	1.5217
CH ₃	55 ^b	106–108	0.4	1.5111
C ₂ H ₅	78	96–97	0.05	1.5052
allyl	78	115	0.1	1.5136
<i>n</i> -C ₃ H ₇	66	154	10	1.5024
<i>n</i> -C ₄ H ₉	73	136	1.5	1.4969
<i>i</i> -C ₄ H ₉	73	128–129	0.3	1.4976
<i>n</i> -C ₅ H ₁₁	83	114–115	0.1	1.4959
<i>i</i> -C ₅ H ₁₁	73	103–104	0.2	1.4988
<i>n</i> -C ₆ H ₁₃	84	133–134	0.4	1.4942
C ₆ H ₅ —CH ₂	86	153–154 ^c	0.2	1.5543

^a Excess (100 %) of sodium compound to benzoyl peroxide.^b Based on consumed benzoyl peroxide.^c Melting point: 58.5–59°C (from pet. ether).

merization products were prepared and VPC analysis of these with the corresponding acyloins from the benzoyl derivatives definitely showed different retention times.

The above method of preparing acyloins from β -ketoesters seems to be without precedent and, starting from easily available chemicals, different α -ketols are produced. Very little work has hitherto been done on *t*-butyl acetoacetate and *t*-butyl esters of other β -ketoacids have not been investigated; it would therefore be of interest to know more about this type of compound and further work is planned to examine the generality of the method presented in this paper.

$$\begin{array}{c} \text{O} \quad \text{R} \\ \parallel \quad | \\ \text{CH}_3\text{C}-\text{CH}-\text{OCOC}_6\text{H}_5 \end{array}$$

Table 4. Analyses of *O*-benzoyl acyloins: $\text{CH}_3\text{C}-\text{CH}-\text{OCOC}_6\text{H}_5$

R	Formula	Calc		Found	
		C	H	C	H
H	C ₁₀ H ₁₀ O ₃	67.40	5.66	67.45	5.68
CH ₃	C ₁₁ H ₁₂ O ₃	68.73	6.29	68.62	6.34
C ₂ H ₅	C ₁₂ H ₁₄ O ₃	69.88	6.84	69.27	6.92
allyl	C ₁₃ H ₁₄ O ₃	71.54	6.47	71.51	6.54
<i>n</i> -C ₃ H ₇	C ₁₃ H ₁₆ O ₃	70.89	7.32	70.74	7.53
<i>n</i> -C ₄ H ₉	C ₁₄ H ₁₈ O ₃	71.77	7.74	71.58	7.83
<i>i</i> -C ₄ H ₉	C ₁₄ H ₁₈ O ₃	71.77	7.74	72.02	8.12
<i>n</i> -C ₅ H ₁₁	C ₁₅ H ₂₀ O ₃	72.55	8.12	72.55	8.19
<i>i</i> -C ₅ H ₁₁	C ₁₅ H ₂₀ O ₃	72.55	8.12	71.99	8.35
<i>n</i> -C ₆ H ₁₃	C ₁₆ H ₂₂ O ₃	73.25	8.45	72.81	8.45
C ₆ H ₅ —CH ₂	C ₁₇ H ₁₆ O ₃	76.10	6.01	75.97	5.83

Experimental

Benzoyl peroxide was recrystallized from chloroform and methanol at low temperature. M.p. 103–104°C (dec). Analyses were made by the Analytical Department of Uppsala University and Dr. A. Bernhardt, Mülheim (Ruhr). Boiling and melting points are not corrected.

Alkylation of t-butyl acetoacetate

As all alkylations were made according to the same procedure only one experiment is described here. Alkyl bromides were used in all cases except two, where methyl iodide and benzyl chloride were more suitable.

t-Butyl- α -n-amylacetoacetate

To a sodium alcoholate solution prepared from 6.9 g of sodium in 150 ml of absolute ethyl alcohol, 47.4 g (0.3 mole) of *t*-butyl acetoacetate are added. After 10 minutes, 45.3 g (0.3 mole) of redistilled *n*-amyl bromide are added dropwise for 25 minutes and then the mixture is refluxed. The excess ethanol is then immediately stripped off at reduced pressure, and the remainder poured into water. The waterphase is twice extracted with ether, and the combined ether extracts washed with water until neutral and then dried over sodium sulphate. Distillation gives the main fraction at b.p. 120–122°C/10 mm Hg (Found: C 67.85, H 10.57; Calc.: C 68.38, H 10.59), $n_D^{20} = 1.4308$. Weight 46 g, yield 67 %.

Preparation of O-benzoyl acyloins

The procedure is the same and only one example is recorded.

Octane-2-one-3-ol-benzoate

In a 1 l three-necked flask, fitted with a mechanical stirrer, a reflux condenser and a dropping funnel, are placed 4.8 g of sodium hydride covered with 200 ml of dry benzene. 45.6 g (0.2 mole) of *t*-butyl- α -n-amylacetoacetate are added dropwise to the sodium hydride, and after 2 h of rapid stirring almost all hydride has reacted, the evolution of hydrogen has ceased and a clear solution has been formed. Then the flask is cooled in an ice-water bath to about 0° and 36.3 g (0.15 mole) of benzoyl peroxide in 200 ml of dry benzene is added dropwise through the dropping funnel during 45 minutes. After another 15 minutes, the peroxide test is negative and the porridge-like mixture is poured into water. The benzene phase is separated, the water phase extracted once with ether and the combined organic extracts washed neutral with water; 15.2 g of benzoic acid is isolated. From the organic phase, solvents and excess starting material are distilled off. To the residue, 0.25 g *p*-toluenesulphonic acid is added. The distillation vessel is connected to a water pump and warmed on an oil bath maintained at a temperature of 160°C. When the decomposition is complete (constant pressure), the product is distilled. The main fraction is obtained at b.p. 114–115°C/0.1 mm Hg (Found: C 72.55, H 8.19; Calc.: C 72.55, H 8.12), $n_D^{20} = 1.4959$. Weight 31 g, yield 83 %.

Hydrolysis experiments

Pentane-2-one-3-ol

41.2 g (0.2 mole) of pentane-2-one-3-ol benzoate were placed in a flask fitted with a mechanical stirrer and a reflux condenser; 350 ml of 5 % sodium hydroxide solu-

tion were added and gentle heat applied (the inner temperature of the flask was 50–60°C) for 25 minutes. Stirring was continued for another half an hour, after which continuous ether extraction was made for 24 hours. From the water phase a quantitative yield of benzoic acid was isolated. The ether phase was washed with cold water, dried over anhydrous sodium sulphate and distilled. 11.3 g (55 %) of pentane-2-one-3-ol with b.p. 41–43°C/10 mm Hg, $n_D^{20} = 1.4227$, were obtained

Anal. $C_5H_{10}O_2$:

Calc.	C 58.80,	H 9.87
Found	C 59.00,	H 10.01

Octane-2-one-3-ol

49.6 g (0.2 mole) of octane-2-one-3-ol benzoate was heated (50°C) with 400 ml of 5 % sodium hydroxide solution for half an hour and the solution stirred until it had reached room temperature. Continuous extraction overnight yielded, after the usual work up, 19.8 g (70 %) of octane-2-one-3-ol. B.p. 90–91°C/10 mm Hg, $n_D^{20} = 1.4340$ (isolated benzoic acid = 24 g).

Anal. $C_8H_{16}O_2$:

Calc.	C 66.63,	H 11.18
Found	C 66.57,	H 11.03

Heptane-1-methyl-5-ol-6-one

49.6 g (0.2 mole) of heptane-2-methyl-5-ol-6-one benzoate was hydrolyzed as above and extracted continuously overnight. 19 g (67 %) of the acyloin was isolated with b.p. 87–88°C/15 mm Hg, $n_D^{20} = 1.4333$.

Anal. $C_8H_{16}O_2$:

Calc.	C 66.63,	H 11.18
Found	C 66.91,	H 10.97

Nonane-2-one-3-ol

26.2 g (0.1 mole) of the corresponding benzoate were heated for 30 minutes with 250 ml of 5 % sodium hydroxide solution and worked up as above. Quantitative yields of benzoic acid and 9.5 g (60 %) of nonane-2-one-3-ol were produced. B.p. 107–108°C/13 mm Hg, $n_D^{20} = 1.4390$.

Anal. $C_9H_{18}O_2$:

Calc.	C 68.31,	H 11.47
Found	C 67.89,	H 11.22

Pentane-2-ol-3-one

Ethylmagnesium bromide was prepared from 24 g of magnesium and 98 g of ethyl bromide in 225 ml of ether. 25 g (0.35 mole) of lactonitrile in 30 ml of dry ether were added to the Grignard reagent, and after the exothermic reaction had subsided, gentle reflux was maintained for 2 hours. The mixture was poured into dilute hydrochloric acid and extracted many times with ether. The combined ether layers were washed with water, dried and distilled. 3.8 g (11 %) of the acyloin were obtained. B.p. 45–47°C/10 mm Hg, $n_D^{20} = 1.4218$.

Anal. $C_5H_{10}O_2$:

Calc.	C 58.80,	H 9.87
Found	C 58.97,	H 9.88

Heptane-2-methyl-5-one-6-ol

iso-Amylmagnesium bromide was prepared from 36 g of magnesium and 183 g of iso-amyl bromide in 350 ml of ether. 27 g (0.38 mole) of lactonitrile in 35 ml of ether were added dropwise and the mixture then refluxed for 2 hours. The usual work-up gave 27 g (54 %) of the acyloin, b.p. 80°C/10 mm Hg, $n_D^{20} = 1.4315$.

Anal. $C_8H_{16}O_2$:

Calc. C 66.63, H 11.18

Found C 66.65, H 11.28

SUMMARY

t-Butyl acetoacetate has been alkylated in ethanol without observed transesterification. The benzoyloxy group has been introduced into a series of alkyl substituted *t*-butyl acetoacetates and, by decomposition of the *t*-butyl esters in the presence of catalytic amounts of *p*-toluenesulphonic acid, the corresponding *O*-benzoyl acyloins have been obtained. Hydrolysis of the *O*-benzoyl derivatives with dilute sodium hydroxide solution gave the acyloins.

ACKNOWLEDGEMENTS

The authors are indebted to Professor A. Fredga, Head of this Institute, for facilities put at their disposal and for his kind interest in this work. Grants from *Statens Naturvetenskapliga Forskningsråd* and *Lucidol Division, Wallace and Tiernan, Inc., Buffalo, N.Y.* are gratefully acknowledged.

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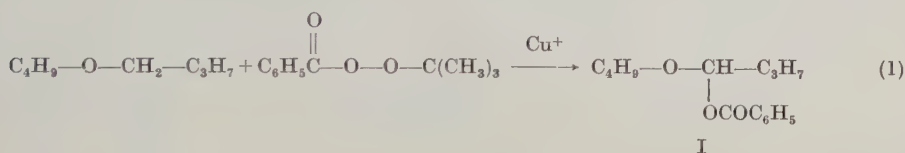
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Studies on peroxy compounds

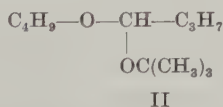
XVIII. The preparation of aldehydes and ketones from ethers^{1,2}

By SVEN-OLOV LAWESSON and CURT BERGLUND

Sosnovsky [1] in the U.S.A. and the present authors [2, 3] in Sweden studied the copper-salt catalyzed decomposition of *t*-butyl perbenzoate in different ethers and it was found [2, 3] that the benzoyloxy group could be introduced into di-*n*-butyl ether according to the following:



Sosnovsky [1] was unable to get a pure sample of I for analytical purposes, but isolated an acetal which, without proof, was given the structure II



Lawesson and Berglund [3] also found a pre-fraction in the same reaction (eqn. 1) but did not give any definitive structure as nothing was known about possible fragmentation of the *n*-butyl ether under these conditions. However, I was refluxed with *t*-butanol and a product was isolated having a refractive index which did not check with that recorded by Sosnovsky. Preliminary hydrolysis experiments of the acetal showed that both *n*-butyl alcohol and *t*-butyl alcohol were present and the product was therefore concluded to be mainly the unsymmetrical acetal II.

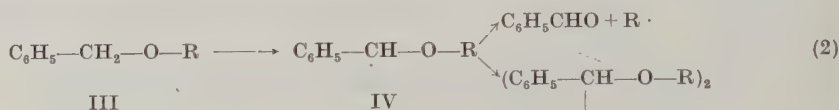
Still earlier, Lawesson and Berglund [4] found that dibenzyl ether, when reacted with *t*-butyl perbenzoate in the presence of catalytic amounts of cuprous chloride, did not give any isolatable acetal and the main product was benzaldehyde dibenzyl-

¹ Part XVII. Lawesson, S.-O., Grönwall, S., and Andersson, M., Arkiv Kemi 17, 457 (1961).

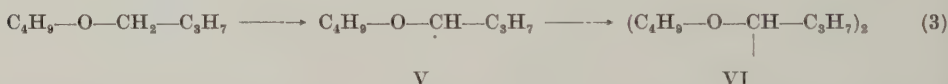
² Preliminary report. Lawesson, S.-O., and Berglund, C., Angew. Chem. 73, 65 (1961).

acetal. No mechanism could be proposed at that time; however, when it was found that benzyl alcohol [5] also gave benzaldehyde dibenzylacetal under the same conditions and that the benzoyloxy derivative of benzyl ethyl ether with ethanol gave benzaldehyde diethylacetal, a mechanism was advanced involving oxygen-alkyl cleavage as a key-step in the series of reactions. Sosnovsky, in an attempt to explain the formation of II, assumed that the acylal I was first formed and this in turn split off benzoic acid giving an unsaturated ether. The subsequent addition of *t*-butanol to the unsaturated ether, under acidic conditions, was then said to give II.

It is known from Huang's work [6] that, when *t*-butyl peroxide is decomposed in the presence of ethers (III), the radical (IV) formed either dimerizes, fragments, or both



No benzyl alcohol was recorded in any experiments. To the present authors' knowledge no similar investigation has been made with simple aliphatic ethers. Earlier, however, Cass [7] studied the decomposition of benzoyl peroxide in diethyl ether which gave 1-ethoxyethyl benzoate and benzoic acid as major products; the kinetics of this reaction were elucidated by Cass [8] and also by Nozaki and Bartlett [9]. We therefore decomposed *t*-butyl peroxide in *n*-butyl ether and the dimer VI was the only product isolated.

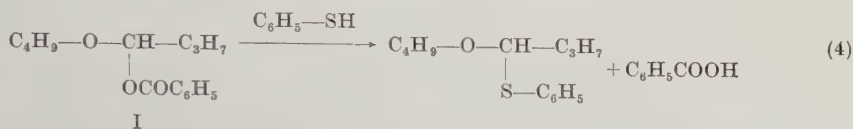


VPC analysis of the pre-fractions, showed that no *n*-butyl alcohol, *n*-butyraldehyde or *n*-octane were present, indicating that the intermediate radical V did not show any tendency to fragment in either direction.

From the above, it is clear that an ether radical, when completely free, either fragments (eqn. 2) or dimerizes (eqns. 2 and 3), and that the formation of the benzaldehyde dibenzyl acetal from benzyl ether must be due to the reaction of the acylal with present alcohols. It is furthermore not necessary that *t*-butanol is the only alcohol present when di-*n*-butyl ether is reacting with *t*-butyl perbenzoate and it is thus not obvious that II, proposed by Sosnovsky, is the isolated acetal. We therefore preliminarily analyzed the alcohol pre-fraction from the reaction between *t*-butyl perbenzoate and *n*-butyl ether and found that not only *t*-butanol was present but also *n*-butyl alcohol. It was consequently felt that a reinvestigation was needed in order to elucidate the encountered problems.

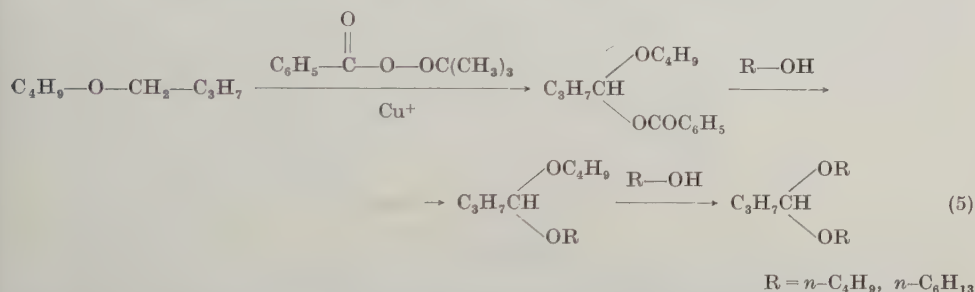
In an earlier investigation of this series [3], it was found that the α -benzoyloxy compound of, for instance, di-*n*-butyl sulphide easily undergoes a 1,2-elimination on heating, giving the α - β -unsaturated sulphide. The same derivative of *n*-butyl ether, on the other hand, gave only benzoic acid and ill-defined products. No vinyl ether could be isolated and, as in this experiment more severe conditions were adopted than in the copper salt catalyzed decomposition of peresters, the postulate [1] by Sosnovsky is subject to doubt. Instead, an oxygen-alkyl cleavage is more plausible.

As in such reactions the carboxylate ion is the departing group, the ether group has to form a relatively stable carbonium ion which, with alcohols, leads to etherification, and, with mercaptans [10], gives the corresponding sulphide. By reacting I with thiophenole 1-butoxy-1-phenylmercapto-butane was isolated in high yields, clearly



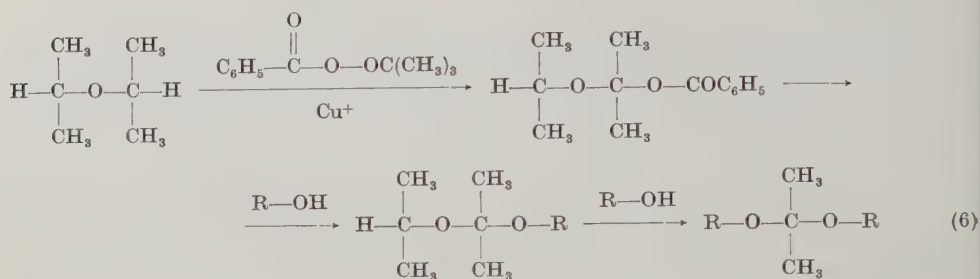
showing that an alkyl-oxygen cleavage mechanism is possible with the acylal I and similar derivatives.

As an acetal was easily formed directly from an ether [1, 2, 3] without first isolating the acylal, we reacted di-*n*-butyl ether with *t*-butyl perbenzoate in the presence of catalytic amounts of cuprous chloride and excess of an alcohol (R-OH) and were able to isolate symmetrical acetals from which the aldehyde was prepared in a few

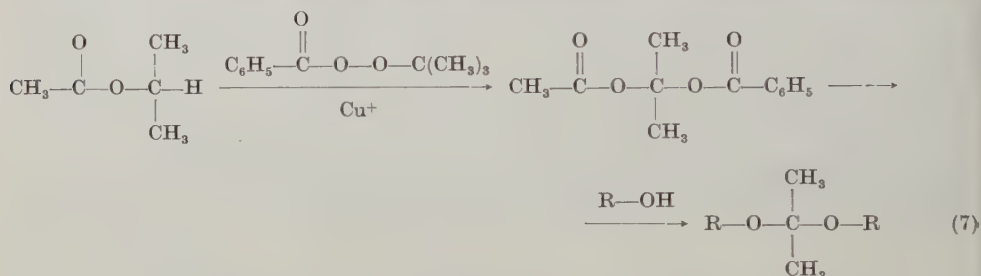


cases. The unsymmetrical acetal, postulated as an intermediate, was not isolated, but was, presumably due to the excess of alcohol present, directly transformed into the symmetrical product; a high yield of the aldehyde derivative was obtained. We also repeated our own [3] and Sosnovsky's [1] experiments, that is, the reactions between di-*n*-butylether and *t*-butyl perbenzoate in the presence of cuprous chloride and cuprous bromide, respectively. The isolated acetal, in both cases, gave on hydrolysis only *n*-butyl alcohol, indicating that the isolated product is *n*-butylaldehyde di-*n*-butylacetal. Benzyl ethers were also investigated, and found to react similarly; benzyl iso-propyl ether thus gave with *t*-butyl perbenzoate, cuprous chloride and excess hexanol, benzaldehyde di-*n*-hexylacetal. Dibenzyl ether also gave acetals with different alcohols but these were difficult to separate from the starting material, limiting the utility of the method. However, by hydrolyzing the mixture, benzaldehyde was easily recovered.

From earlier work [3], it is known that ethers or sulphides with a tertiary hydrogen on an α -carbon, do not give any well-defined products when reacted with *t*-butyl perbenzoate, the formed primary products presumably decomposing under the applied conditions. Phenyl-*i*-propyl ether and phenyl *i*-propyl sulphide did not leave any products in the presence of alcohols but di-*i*-propyl ether in the presence of alcohols gave symmetrical ketals of acetone; the unsymmetrical intermediate could not be isolated as, with the excess of alcohol present, it gave the symmetrical derivative.



We also reacted *i*-propyl acetate with *t*-butyl perbenzoate in the presence of *n*-butyl alcohol and isolated, acetone di-*n*-butyl ketal. It seems clear that the tertiary hydrogen is first abstracted, after which the acylal with the alcohol gives the ketal:



Experimental

The reactions were carried out in an atmosphere of dry, oxygen-free, nitrogen. All ethers were distilled immediately before use. The *t*-butylperbenzoate (Light; $n_D^{20} = 1.5000$) was used in all experiments without further purification except drying over sodium sulphate. The rate of the decomposition of the perester was followed by titration according to the method of Silbert and Swern [11]. The infrared measurements were made on an Infracord. The analysis were made by the Analytical Department, Uppsala University. Boiling points are uncorrected.

Starting material

Commercial di-*n*-butyl ether, di-*i*-propyl ether and *i*-propyl acetate were used. Benzyl *i*-propyl ether [12] was prepared from benzyl chloride and sodium *i*-propylate and dibenzyl ether [4] from benzylalcohol.

The reaction of *t*-butyl perbenzoate with di-*n*-butyl ether according to Sosnovsky

t-Butyl perbenzoate (0.10 mole) was added dropwise for 25 minutes to a refluxing benzene solution (100 ml), containing 0.35 mole of redistilled di-*n*-butyl ether and 0.1 g of cuprous bromide. After refluxing for 48 hours at 90°C, the reaction was stopped. The reaction mixture, diluted with ether, was washed with 2 *M* NaOH, then with water, and finally dried over sodium sulphate. The alkaline solution was acidified and the precipitated benzoic acid was found to weigh 9.3 g. From the organic solution, benzene and the excess of di-*n*-butyl ether were removed under

reduced pressure. The pre-fractions were analyzed by VPC and it was shown that *n*-butanol was present. At 93°C/10 mm Hg 6 g of the acetal were obtained ($n_D^{20} = 1.4182$). Yield 30 %.

Anal. $C_{12}H_{26}O_2$ (202.33)

Calc. C 71.23, H 12.95

Found C 71.23, H 12.75

Hydrolysis of the acetal

3 g of the acetal and 6 ml of 2 *M* H_2SO_4 were refluxed for 2 hours at a temperature of 110°C. The mixture was dissolved in ether, washed until neutral and dried. VPC analysis of the hydrolysate showed *n*-butanol to be the only alcohol present.

The reaction of t-butyl perbenzoate with di-n-butyl ether in the presence of t-butanol

t-Butyl perbenzoate (0.2 mole) was added dropwise during a period of 40 minutes to a refluxing benzene solution (100 ml) containing 0.5 mole of di-*n*-butyl ether, 0.5 mole of *t*-butanol and 0.1 g of cuprous chloride. After refluxing for 27 hours at 81°C, the reaction mixture was cooled down to room temperature, washed with 2 *M* NaOH and water, and finally dried over sodium sulphate. The precipitated benzoic acid weighed 14.1 g. Fractionation gave 11.5 g of the acetal with a b.p. of 83°/10 mm Hg; $n_D^{20} = 1.4182$. The yield was 48 % calculated on the obtained benzoic acid. The distillation residue, mainly the benzoyloxy compound, weighed 19 g.

Anal. $C_{12}H_{26}O_2$ (202.33)

Calc. C 71.23, H 12.95

Found C 71.05, H 12.87

Hydrolysis of the acetal

6 g of the acetal were refluxed for 2 hours with 10 ml of 2 *M* H_2SO_4 at a temperature of 110°C. The mixture was then dissolved in ether, washed with sodiumbicarbonate and water, and finally dried over sodium sulphate. Distillation gave a fraction with b.p. 75–120°C at normal pressure, and showed according to the VPC analysis sharp peaks (1:1) for *n*-butanol and *t*-butanol.

The reaction of α-benzoyloxy di-n-butyl ether with t-butanol

α-Benzoyloxy di-*n*-butyl ether, 25 g (0.1 mole), $n_D^{20} = 1.4837$, was refluxed with *t*-butanol (0.2 mole) in 50 ml of benzene for 6 hours at 85°C. The work-up was performed as usual, yielding 7.5 g of benzoic acid. The acetal, 12 g (58 %), was obtained at 90°/10 mm Hg; $n_D^{20} = 1.4188$.

Anal. $C_{12}H_{26}O_2$ (202.33)

Calc. C 71.23, H 12.95

Found C 71.08, H 12.94

Hydrolysis of the acetal

8 g of the acetal were refluxed with 10 ml of 2 *M* H_2SO_4 for 2 hours at 110°. The mixture was dissolved in ether, washed with sodium bicarbonate and water and dried over sodium sulphate. Distillation gave *n*-butyraldehyde (b.p. 75°) and a fraction with b.p. 75–120°C; VPC analysis showed that fraction to contain equal amounts of *n*-butanol and *t*-butanol.

The reaction of t-butyl perbenzoate with di-n-butyl ether in the presence of n-butanol

t-Butyl perbenzoate (0.2 mole) was added for 35 minutes to a refluxing mixture of di-*n*-butyl ether (200 ml), *n*-butanol (0.5 mole) and cuprous chloride (0.1 g). After refluxing for 5 hours at an oil bath temperature of 91°C, the mixture was worked up as usual. 24 g of benzoic acid were precipitated. After distilling off the excess di-*n*-butyl ether and *n*-butanol, 20 g (50 %) of the acetal, b.p. 98–99°/10 mm Hg, $n_D^{20} = 1.4178$ were obtained.

Preparation of butyraldehyde di-n-butylacetal

Benzene (100 ml), *n*-butanol (0.2 mole), *n*-butyraldehyde (0.1 mole), and 2 ml of conc. HCl were refluxed for 3 hours with a water separator. Fractionation of the neutral and dry solution gave at a b.p. of 98°/10 mm Hg 15 g (74 %) of the acetal; $n_D^{20} = 1.4174$.

Anal. $C_{12}H_{26}O_2$ (202.33)

Calc. C 71.23, H 12.95

Found C 71.23, H 12.96

The IR-spectrum was identical with that from the preceding experiment.

The reaction of t-butyl perbenzoate with di-n-butyl ether in the presence of n-hexanol

To 200 ml of di-*n*-butylether, 68 g of *n*-hexanol and 0.1 g of cuprous chloride, maintained at an oil bath temperature of 87°C, *t*-butyl perbenzoate (0.2 mole) was added for 35 minutes. After heating for 22 hours the mixture was worked up as usual, yielding 24 g of benzoic acid. Fractionation gave 35 g (68 %) of the di-*n*-hexyl acetal of butyraldehyde at a b.p. of 95°/0.05 mm Hg, $n_D^{20} = 1.4346$.

Anal. $C_{18}H_{34}O_2$ (258.43)

Calc. C 74.36, H 13.26

Found C 74.37, H 12.90

The IR-spectrum was identical with that of authentic butyraldehyde di-*n*-hexylacetal.

Preparation of butyraldehyde di-n-hexylacetal

Anhydrous benzene (100 ml), *n*-hexanol (0.2 mole), butyraldehyde (0.1 mole) and 2 ml of conc. HCl, were refluxed for 3 hours with a water separator. The solution was washed, dried and distilled. The acetal was obtained at 175°C/20 mm Hg, $n_D^{20} = 1.4343$. 19.5 g (76 %).

The reaction of α-benzoyloxy-di-n-butyl ether with thiophenole

25 g (0.1 mole) of the benzoyloxy compound were refluxed for 6 hours at 93°C with 22 g (0.2 mole) of thiophenole in 100 ml of anhydrous benzene.

The work-up was performed in the usual way, giving 9 g of benzoic acid. Fractionation gave 15 g (59 %) 1-*n*-butoxy-1-phenylmercapto-butane at a b.p. of 93°/0.2 mm Hg.

Anal. $C_{14}H_{22}OS$ (254.38)

Calc. C 70.55, H 9.31, S 13.41

Found C 70.61, H 9.04, S 13.23

The reaction of di-t-butylperoxide with di-n-butyl ether

75 ml of di-*n*-butyl ether and 8 g of di-*t*-butyl peroxide were refluxed at 140° for a period of 14 hours. Fractionation gave 4 g of the dimer of di-*n*-butyl ether. B.p.

133°/20 mm Hg, $n_D^{20} = 1.4300$. The VPC diagram of the fore-runs showed that *n*-butanol was absent.

Anal. $C_{16}H_{34}O_2$ (258.43)

Calc. C 74.36, H 13.26

Found C 74.60, H 12.99

The reaction of t-butyl perbenzoate with di-i-propyl ether in the presence of n-butanol

0.2 mole of *t*-butyl perbenzoate was added dropwise to 200 ml of di-*i*-propyl ether, 0.5 mole of *n*-butanol and 0.1 g of cuprous chloride. The solution was maintained at a gentle reflux for 17 hours. After washing and drying in the usual manner, 24 g of benzoic acid precipitated. Fractionation of the organic phase gave 11.5 g (31 %) of acetone di-*n*-butylketal, b.p. 70–71°/10 mm Hg, $n_D^{23} = 1.4145$. Lit. [13]: B.p. 64–64.5°/3 mm Hg, $n_D^{20} = 1.4120$. The VPC analysis of this product showed the same retention time as that of authentic acetone di-*n*-butylketal.¹

Anal. $C_{11}H_{24}O_2$ (188.30)

Calc. C 70.16, H 12.85

Found C 70.08, H 12.83

The reaction of t-butyl perbenzoate with di-i-propyl ether in the presence of n-hexanol

0.2 mole of *t*-butyl perbenzoate was added for 45 minutes to a mixture of 200 ml of di-*i*-propyl ether, 0.5 mole of *n*-hexanol and 0.1 g of cuprous chloride, maintained at an oil bath temperature of 79°C. The reaction was ended after 21 hours, whereupon the mixture was worked up, giving 16 g (33 %) of acetone di-*n*-hexylketal, b.p. 120°/10 mm Hg, $n_D^{20} = 1.4336$.

Anal. $C_{15}H_{32}O_2$ (244.41)

Calc. C 73.71, H 13.20

Found C 73.48, H 12.94

The reaction of t-butyl perbenzoate with benzyl i-propyl ether in the presence of n-hexanol

150 ml of benzene, 60 g of benzyl *i*-propyl ether, 50 ml of *n*-hexanol and 0.1 g of cuprous chloride were placed in the reaction flask, maintained at an oil bath temperature of 83°C. 0.2 mole of *t*-butyl perbenzoate, dissolved in 50 ml of benzene was added dropwise for half an hour. The solution was maintained at gentle reflux for 23 hours and then worked up as usual, giving 24 g of benzoic acid from the alkaline washings. Distillation gave 19 g (33 %) of the benzaldehyde di-*n*-hexylacetal. B.p. 125°/0.1 mm Hg, $n_D^{20} = 1.4747$.

Anal. $C_{19}H_{32}O_2$ (292.45)

Calc. C 78.03, H 11.03

Found C 77.90, H 11.03

Preparation of benzaldehyde di-n-hexylacetal

Benzene (250 ml), *n*-hexanol (0.2 mole), benzaldehyde (0.1 mole) and conc. HCl (1 ml) were refluxed for 4 hours in a flask equipped with a water separator. The neutral, dry solution gave 9 g (31 %) of the acetal. B.p. 125°/0.1 mm Hg, $n_D^{20} = 1.4749$.

IR-spectra were identical from the two preparations.

¹ Generously supplied by the Dow Chemical Company, Midland, Mich., USA.

*The reaction of *t*-butyl perbenzoate with benzyl *i*-propyl ether in the presence of *n*-butanol*

0.2 mole of *t*-butyl perbenzoate was added dropwise for 55 minutes to a mixture of 150 ml of benzene, 60 ml of *n*-butanol and 0.1 g of cuprous chloride, maintained at 85°C. The reaction was stopped after 21 hours. The alkaline washings gave quantitative yields of benzoic acid (24 g). After drying and distilling off the benzene and excess of benzyl *i*-propyl ether and *n*-butanol, 5.1 g (11 %) of the benzaldehyde di-*n*-butylacetal were produced, b.p. 145–150°/10 mm Hg, $n_D^{20} = 1.4786$. Lit. [14]. B.p. 140–145°/10 mm Hg, $n_D^{20} = 1.4770$.

*The reactions of *t*-butyl perbenzoate with dibenzyl ether in the presence of alcohols*

t-Butyl perbenzoate (0.2 mole) was added dropwise to dibenzylether (70 g) and 0.1 g of cuprous chloride in 200 ml of anhydrous benzene; an alcohol [ROH, (R = C₂H₅, *i*-C₃H₇, *n*-C₄H₉)] in great excess was also present. The temperature of the oil bath was maintained between 90 and 100°. The reaction time was 16 hours. In each attempt, a quantitative amount of benzoic acid was obtained. When the mixtures were distilled, however, it was impossible to obtain the benzaldehyde acetals in a pure form, as they all had a boiling point about the same as that for the benzylether. Infrared and gas chromatography analysis showed that an acetal was present. In the case of the di-*n*-butylacetal of benzaldehyde, a hydrolysis was performed and this mixture was shown by vapour phase chromatography analysis to contain *n*-butanol and benzaldehyde.

*The reaction of *t*-butyl perbenzoate with *i*-propyl acetate in the presence of *n*-hexanol*

0.4 mole of *i*-propyl acetate, 0.4 mole of *n*-hexanol and 0.1 g of cuprous chloride in 150 ml of benzene were heated to 83°C and 0.2 mole of *t*-butyl perbenzoate was then added dropwise for 45 minutes. After 17 hours, the reaction was stopped and 24 g of benzoic acid were obtained from the alkaline washings. Fractionation gave 6 g (12%) of acetone di-*n*-hexylketal, b.p. 120°/13 mm Hg, $n_D^{20} = 1.4342$. The IR-spectrum was identical with that from the reaction between *t*-butyl perbenzoate, di-*i*-propyl ether and *n*-hexanol.

SUMMARY

It has been found that when *n*-butyl ether is treated with *t*-butyl peroxide, it gives a dimer and no fragmentation of the intermediate ether radical is observed. Cuprous chloride catalyzed decomposition of *t*-butyl perbenzoate in the presence of di-*n*-butyl ether gives the primary product 1-*n*-butoxy-1-benzoyloxy-butane which, in the presence of different alcohols, gives symmetrical acetals. Ketals are also formed from di-*i*-propyl ether by the same method.

ACKNOWLEDGEMENTS

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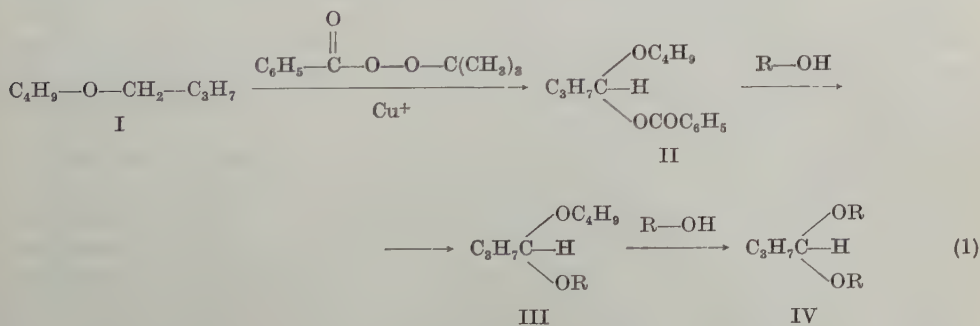
Tryckt den 4 maj 1961

Uppsala 1961. Almqvist & Wiksells Boktryckeri AB

XIX. The reaction between *t*-butyl perbenzoate and tetrahydrofuran or tetrahydropyran in the presence of alcohols¹

When *t*-butyl perbenzoate is decomposed in the presence of a cuprous salt, the oxygen-oxygen bond is broken and *t*-butoxy and benzoyloxy radicals are formed. With compounds containing activated hydrogens, the *t*-butoxy radical removes a hydrogen followed by combination of the benzoyloxy radical with the new radical, forming a benzoate. It has been postulated that the copper salt present in these reactions stabilizes the intermediate radical, thus preventing isomerization of olefins [1, 2], fragmentation or dimerization of benzyl ethers [3, 4], benzyl sulphides [5] or aliphatic ethers and sulphides [6]; the copper salt also increases the rate of decomposition of the perester, thereby making it suitable as a synthetic tool. Two mechanisms have been put forward [2, 7] neither of which at present can be definitely rejected.

Quite recently [8, 9], the present authors described a method of preparing aldehyde and ketone derivatives from ethers by copper salt catalyzed decomposition of *t*-butyl perbenzoate in the presence of alcohols:



n-Butyl ether, I, which was extensively investigated, thus gave *n*-butyraldehyde dialkylacetal, IV, in fair yields; it was possible to isolate the intermediate acylal, II, but it was sensitive to oxygen. The unsymmetrical acetal, III, was not isolated as

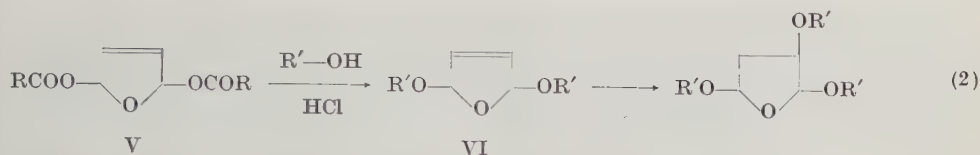
¹ Part XVIII. Ref. [9].

it was presumably transformed to the symmetrical compound. As II on heating gave no detectable vinyl ether, an oxygen-alkyl heterolysis seems to be more plausible than a primary elimination of benzoic acid followed by addition of the corresponding alcohol to the unsaturated ether. Similarly, symmetrical ketals were prepared from di-*i*-propyl ether and an oxygen-alkyl heterolysis was also proposed in this case. Finally, the isolation has earlier been recorded of acetals from the reaction of *t*-butyl perbenzoate and dibenzyl ether [4] or benzyl alcohol [5]. As with certain cyclic ethers, acetals are also formed [10], that work has been extended [11] and the full details of the work with tetrahydrofuran and tetrahydropyran are described in this paper.

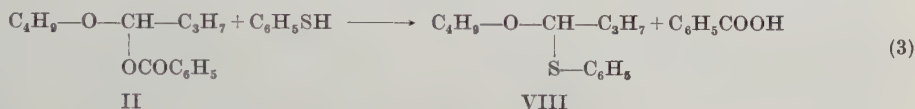
It is known from different investigations on simple ethers that a free radical abstracts an available hydrogen in the α position to a hetero atom. With cyclic ethers this would also be the case, and Cass [12] prepared 2-benzoyloxy-1,4-dioxane from dioxane and benzoyl peroxide; Sosnovsky [13] and the present authors [10] prepared the same compound by the copper salt catalyzed decomposition of *t*-butyl perbenzoate and also other types of cyclic ethers [14] have been found to react similarly with *t*-butyl perbenzoate. With tetrahydrofuran, only 2-*t*-butoxy tetrahydrofuran was isolated as the reaction product, which was quite unexpected. Vapour phase chromatography (VPC) of the product showed only one sharp peak and it was concluded that the alkoxy group had entered an α -position. By NMR spectroscopy it was also shown that the isolated product was substituted in the 2-position and finally, by an unequivocal synthesis, 2-*t*-butoxy tetrahydrofuran was made by addition of *t*-butanol to 2,3-dihydrofuran.

The general procedure for the reaction between tetrahydrofuran and *t*-butyl perbenzoate in the presence of catalytic amounts of cuprous chloride was to add the diluted perester to a preheated solution of the substrate. By experience it was known that α -benzoyloxy ethers fragment at high temperature and, finding that quantitative yields of benzoic acid were isolated in our first experiments, all reactions were thereafter performed at a rather low temperature. After all the perester had been consumed (determined by periodical infrared analyses), the reaction was allowed to continue for another 15 minutes and was then immediately worked up in the usual way. Almost quantitative yields of benzoic acid were isolated irrespective of the reaction temperature; after the acetal had been distilled off from the neutral phase, there remained a neutral residue in each case, which, on attempted distillation, decomposed partly into benzoic acid. Crystallization of the residue was unsuccessful. It is therefore clear from this and other similar experiments that with tetrahydrofuran an α -hydrogen is first abstracted, followed by the combination of the benzoyloxy radical with the ether radical, giving a benzoate.

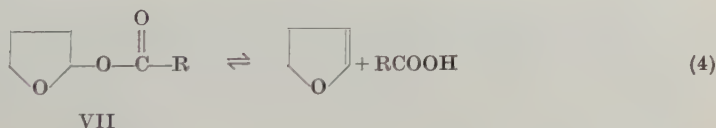
The question arises as to how the benzoyloxy group is exchanged and the *t*-butoxy group introduced. However, the literature regarding 2-acyloxy tetrahydrofurans is very limited in this respect. Normant [15] added acetic acid to 2,3-dihydrofuran and obtained 2-acetoxy tetrahydrofuran, Reppe [16] treated, 2,3-dichloro tetrahydrofuran with glacial acetic acid to obtain 2-acetoxy-3-chloro tetrahydrofuran and Gross [17] prepared 2,5-diacetoxy tetrahydrofuran (b.p. 123–125°C/8 mm Hg) from sodium acetate and 2,5-dichloro-tetrahydrofuran and all of these compounds seem to be stable on distillation. A similar type of compound, 2,5-diacyloxy-2,5-dihydrofuran V, was prepared by Clauson-Kaas [18] and later by Stoll *et al.* [19] from furan and carboxylic acids; these compounds underwent an exchange reaction when treated with alcohols and with hydrogen halides present react according to the following scheme:



The exchange of acyloxy groups with alkoxy-ones in this case is only possible through an alkyl-oxygen cleavage, which presumably is facilitated as the α -positions are also activated by the double bond. A similar mechanism is also plausible with 2-benzoyloxy tetrahydrofuran, VII ($\text{R}=\text{C}_6\text{H}_5$). This suggestion is partly based on recent results [8, 9] with alkyl ethers (eqn. 1), where the reaction between an acylal II, and alcohols gave acetals; with II, thiophenol also gave the corresponding sulphur compound, VIII:

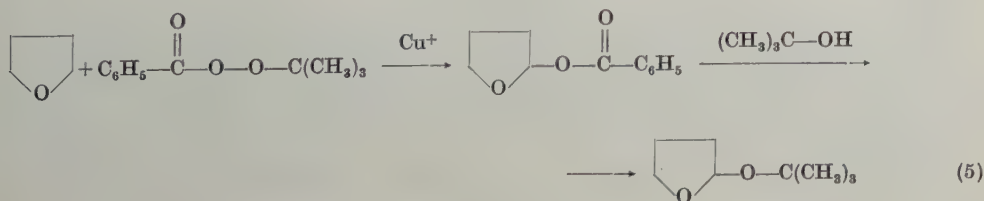


In these cases, a 1,2 elimination is improbable as an addition of alcohols to simple non-cyclic vinyl ethers under the applied conditions has not been observed, as far as is known. However, with a cyclic vinyl ether such as 1,2-dihydrofuran, addition of alcohols to the double bond occurs easily and, if the 2-benzoyloxy tetrahydrofuran can fragment giving benzoic acid and dihydrofuran, the mechanism proposed by Sosnovsky is feasible. We believe that an equilibrium may exist between dihydrofuran and an acid as follows and that, at increased temperature, VII may

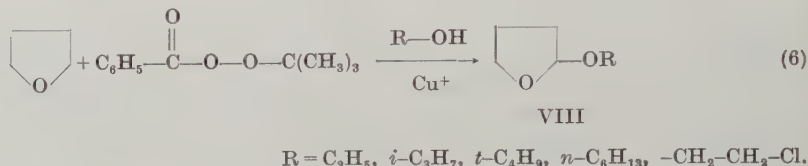


decompose; it is not clear, however, whether VII, when heated at 80°C with *t*-butanol in a strictly neutral medium, would give the cyclic acetal mainly according to the Sosnovsky mechanism. The oxygen-alkyl cleavage is an alternative which should be considered.

When *t*-butyl perbenzoate was decomposed in tetrahydrofuran in the presence of cuprous chloride, only 2-*t*-butoxy tetrahydrofuran was isolated according to the following:

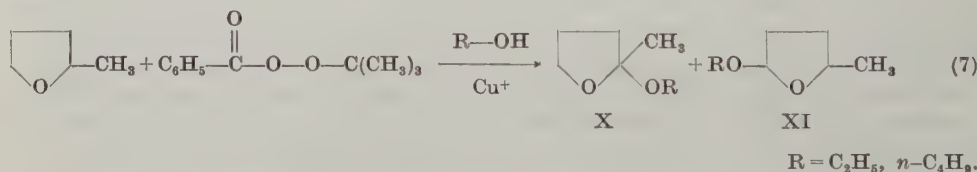


It was also found that, if *t*-butanol was added to the substrate before the perester was allowed to react, the yield of the acetal was increased. Alcohols with α -hydrogens can be attacked by radicals but with *t*-butanol no complication can arise. By addition of other hydroxy compounds to the substrate, as above, different ether groups were introduced into tetrahydrofuran:

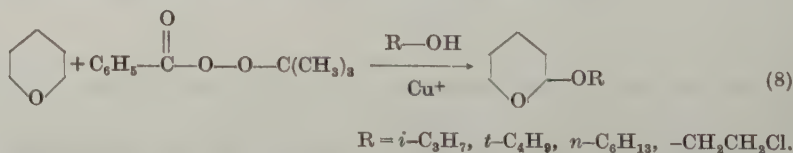


In all these experiments, the added alcohol was present in excess and a reaction between VII ($\text{R} = \text{C}_6\text{H}_5$) and *t*-butanol was not favoured.

2-Methyltetrahydrofuran was also reacted with *t*-butyl perbenzoate but no well-defined product was isolated. However, in the presence of ethanol and *n*-butanol, cyclic acetals were isolated; C,H-analyses showed that one alkoxy group had been introduced and it was reasonable to suppose that the major initial attack occurred at the tertiary hydrogen. However, VPC-analysis showed that 2-butoxy-2-methyltetrahydrofuran [20], X¹, and presumably XI had been formed in about equal amounts.



A similar investigation was also made with tetrahydropyran, and it was found that the *t*-butoxy group was introduced into the 2-position; when different alcohols were present in excess, the corresponding acetals were formed as follows



The corresponding acetals were identified by unequivocal syntheses from the alcohols and 1,2-dihydropyran.

Experimental

The reactions were performed in an atmosphere of oxygen-free nitrogen. Tetrahydrofuran and tetrahydropyran were refluxed over sodium and distilled immediately before use. Commercial *t*-butyl perbenzoate ($n_D^{20} = 1.5000$) from Light Co. was dried over sodium sulphate and used without further purification. The cuprous chloride was

¹ Our cordial thanks are expressed to Dr. A. P. Dunlop of the Quaker Oats Company for supplying this compound.

the ordinary laboratory reagent. No reaction was considered complete unless a negative test for peroxide was obtained. The decomposition rate of the *t*-butyl perbenzoate was followed by periodical measurement on an Infracord spectrophotometer. The analyses were made by the Analytical Department, Uppsala University, the VPC analyses at the same Institute and by Pharmacia AB, Uppsala, and the NMR spectra by the Physics Department, Uppsala University. Boiling points are uncorrected.

The reaction of t-butyl perbenzoate with tetrahydrofuran

A 500 ml three-necked flask was fitted with a mechanical stirrer, a dropping funnel and a reflux condenser, the top of which was connected to a gas collector; 200 ml of tetrahydrofuran ($n_D^{20} = 1.3802$) and 0.1 g of cuprous chloride were placed in the flask. The system was swept with nitrogen gas and the solution warmed to gentle reflux (68°C). 0.2 mole of *t*-butyl perbenzoate in 25 ml of anhydrous benzene were added dropwise over a period of 20 minutes. The reaction was almost complete after 4 hours. The solution was at room-temperature diluted with ether, washed 3 times with 2 *M* NaOH solution, then with water until neutral and dried over sodium sulphate. The acidified alkaline solution gave 17.5 g of benzoic acid. After removing the ether and tetrahydrofuran, a fraction was obtained at 140–141°C. 9 g; yield 31 %; $n_D^{20} = 1.4194$. The compound was shown to be 2-*t*-butoxy tetrahydrofuran by IR and NMR measurements. A distillation residue (7.5 g) containing a benzoate could not be purified.

Anal. C₈H₁₆O₃ (144.21)

Calc. C 66.63, H 11.18

Found C 66.57, H 10.93

The reaction of t-butyl perbenzoate with tetrahydrofuran in the presence of ethanol

108 g (1.5 mole) of tetrahydrofuran, 19 g (0.4 mole) of ethanol and 0.1 g of cuprous chloride were placed in the apparatus described above. 0.2 mole of *t*-butyl perbenzoate in 25 ml of benzene were added for 15 minutes to the tetrahydrofuran-ethanol solution, maintained at an oil bath temperature of 75°C. After 6 hours reflux, the reaction was complete. The work-up was as above, the alkaline washings giving 24 g of benzoic acid. After drying, the solution was distilled and when the ether and the excess tetrahydrofuran and ethanol had been removed, the 2-ethoxy tetrahydrofuran was obtained in a 40 % yield. (9.2 g); $n_D^{20} = 1.4149$. B.p. 125°C.

Anal. C₆H₁₂O₃ (116.16)

Calc. C 62.04, H 10.41

Found C 62.05, H 10.50

The reaction of t-butyl perbenzoate with tetrahydrofuran in the presence of i-propanol

t-Butyl perbenzoate (0.2 mole) was added dropwise to a refluxing tetrahydrofuran solution (108 g, 1.5 mole) containing 24 g (0.4 mole) of *i*-propanol and 0.1 g of cuprous chloride. After refluxing for 13 hours at an oil bath temperature of 80°C, the reaction was complete. The work-up was performed as in previous experiments and the alkaline washings gave 24 g of benzoic acid. Fractionation of the organic phase gave 11.5 g (44 %) of 2-*i*-propoxy tetrahydrofuran at 132°C. $n_D^{20} = 1.4147$.

Anal. C₇H₁₄O₃ (130.18):

Calc. C 64.58, H 10.84

Found C 64.37, H 10.89

The reaction of t-butyl perbenzoate with tetrahydrofuran in the presence of t-butanol

A flask containing 108 g (1.5 mole) of tetrahydrofuran, 50 g (0.68 mole) of *t*-butanol and 0.1 g of cuprous chloride was maintained at an oil bath temperature of 78°C; 0.2 mole of *t*-butyl perbenzoate were added dropwise for 15 minutes. After 12 hours, the reaction was complete. The work-up was performed as usual giving 24 g of benzoic acid and 16.5 g (57 %) of 2-*t*-butoxy tetrahydrofuran. $n_D^{20} = 1.4193$. B.p. 140–141°C.

The reaction of t-butyl perbenzoate with tetrahydrofuran in the presence of n-hexanol

t-Butyl perbenzoate (0.2 mole) was added dropwise to a solution of 108 g (1.5 mole) of tetrahydrofuran, 41 g (0.4 mole) of *n*-hexanol and 0.1 g of cuprous chloride, at an oil bath temperature of 82°C. When the solution had been refluxed for 10 hours, the reaction was complete. 24 g of benzoic acid were obtained. Fractionation of the neutral dry solution gave 18 g (52 %) of 2-*n*-hexoxy tetrahydrofuran at a b.p. of 87°–88°/10 mm Hg.

Anal. $C_{10}H_{20}O_2$ (172.26)

Calc. C 69.72, H 11.70

Found C 69.59, H 11.74

The reaction of t-butyl perbenzoate with tetrahydrofuran in the presence of ethylene chlorohydrin

t-Butyl perbenzoate (0.2 mole) was added dropwise to 200 ml of tetrahydrofuran, 50 ml of redistilled ethylene chlorohydrin ($n_D^{20} = 1.4432$) and 0.1 g of cuprous chloride contained in a flask. After refluxing for 19 hours at 75°C, the reaction was stopped and the work-up performed as usual, but using 2 *M* sodium bicarbonate solution instead of NaOH solution. A quantitative yield (24 g) of benzoic acid was precipitated. Fractionation of the organic phase gave 24 g (80 %) of 2-(β -chloroethoxy)-tetrahydrofuran at 87°/25 mm Hg; $n_D^{20} = 1.4522$.

Anal. $C_6H_{11}O_2Cl$ (150.59)

Calc. C 48.00, H 7.33, Cl 23.33

Found C 47.52, H 7.31, Cl 23.31

Preparations of the 2-alkoxy tetrahydrofurans from 2,3-dihydrofuran and corresponding alcohols

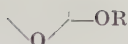
Equimolar quantities of alcohol and 2,3-dihydrofuran¹ ($n_D^{20} = 1.4206$) were shaken at 0°C in the presence of a trace of concentrated hydrochloric acid and allowed to stand for 1 hour. In the case of ethylene chlorohydrin the acid was unnecessary. The reaction was exothermic. A few pellets of sodium hydroxide were then added to the reaction mixture to neutralize the acid. The product was then decanted and isolated directly by distillation. The chlorocompound was, however, washed only with bicarbonate solution and water until neutral and then dried.

The reaction of t-butyl perbenzoate with 2-methyl tetrahydrofuran in the presence of ethanol

t-Butyl perbenzoate (0.2 mole) was added dropwise to a mixture of 87 g (1 mole) of 2-methyl tetrahydrofuran² ($n_D^{20} = 1.4091$), 30 g (0.65 mole) of ethanol and 0.1 g of

¹ Generously supplied by Badische Anilin u. Soda Fabrik A.G., Ludwigshafen am Rhein, Deutschland.

² Generously supplied by the Quaker Oats Company Chemicals Division, Chicago 54, Illinois, U.S.A.



R	B.p. (°C)	mm Hg	n_D^{20}	Yield %
C_2H_5	125	760	1.4148	72
<i>i</i> - C_3H_7	132	760	1.4147	63
<i>t</i> - C_4H_9	141	760	1.4194	28
<i>n</i> - C_6H_{13}	88	10	1.4332	81
$\text{Cl—CH}_2\text{—CH}_2$	83	18	1.4520	74

cuprous chloride at an oil bath temperature of 83°C. The reaction was complete after 5 hours and the mixture worked up as usual, yielding 6.2 g (24 %) of the ethoxy compound of 2-methyl tetrahydrofuran at 129°C. $n_D^{20} = 1.4145$. A quantitative yield of benzoic acid was obtained (24 g).

Anal. $\text{C}_7\text{H}_{14}\text{O}_2$ (130.18)

Calc. C 64.58, H 10.84

Found C 64.57, H 10.93

The reaction of t-butyl perbenzoate with 2-methyl tetrahydrofuran in the presence of n-butanol

86 g (1 mole) of 2-methyl tetrahydrofuran, 40 g (0.55 mole) of *n*-butanol and 0.1 g of cuprous chloride were placed in a flask and 0.2 mole of *t*-butyl perbenzoate added for 30 minutes. The mixture was maintained at gentle reflux at an oil bath temperature of 84°C for 19 hours. After washing and drying in the usual manner, fractionation of the organic phase gave 15.5 g of the *n*-butoxy compounds of 2-methyl tetrahydrofuran (49 %); $n_D^{20} = 1.4209$; b.p. 74°/23 mm Hg. Precipitated benzoic acid: 24 g.

Lit. [20] $n_D^{20} = 1.4230$.

Anal. $\text{C}_9\text{H}_{18}\text{O}_2$ (158.23)

Calc. C 68.31, H 11.47

Found C 68.29, H 11.49

The reaction of t-butyl perbenzoate with tetrahydropyran

200 ml of benzene, 35 g (0.4 mole) of redistilled tetrahydropyran ($n_D^{20} = 1.4216$) and 0.1 g of cuprous chloride were placed in the reaction flask and maintained at an oil bath temperature of 82°C. 30 ml (0.15 mole) of *t*-butyl perbenzoate were added dropwise for 25 minutes. The reaction was complete after 4 hours, and the mixture then worked up as usual, giving 4.5 g of benzoic acid from the alkaline washings. Distillation gave 7.3 g (23 %) of the *t*-butoxy compound ($n_D^{20} = 1.4271$) at 42°–45°/10 mm Hg. The benzoyloxy compound distilled at 70°–90°/0.2 mm Hg, but attempts to obtain this compound in an analytically pure form were unsuccessful.

Sosnovsky [21] has also obtained the *t*-butoxy compound in 33 % yield, $n_D^{20} = 1.4268$ and the b.p. of 56°/13 mm Hg.

The reaction of t-butyl perbenzoate with tetrahydropyran in the presence of n-hexanol

t-Butyl perbenzoate (0.2 mole) was added dropwise to a refluxing benzene solution (100 ml), containing 43 g (0.5 mole) of tetrahydropyran, 51 g (0.5 mole) of *n*-hexanol

and 0.1 g of cuprous chloride. After refluxing for 18 hours, the reaction was stopped and the reaction mixture washed with 2 *M* NaOH solution and water and finally dried over sodium sulphate. The alkaline washings gave 17 g of benzoic acid. Benzene, excess *n*-hexanol and tetrahydropyran were removed from the organic solution under reduced pressure. At 110°C/12 mm Hg. 11 g (30 %) of 2-hexoxy tetrahydropyran was obtained. $n_D^{20} = 1.4382$. Distillation residue: 14 g Lit. [22] $n_D^{20} = 1.4401$.

Anal. $C_{11}H_{22}O_2$ (186.29)

Calc. C 70.92, H 11.90

Found C 70.94, H 11.91

The reaction of t-butyl perbenzoate with tetrahydropyran in the presence of i-propanol

t-Butyl perbenzoate (0.2 mole) was added over a 30 minute interval to a flask containing 43 g (0.5 mole) of tetrahydropyran, 30 g (0.5 mole) of *i*-propanol in 100 ml of anhydrous benzene and 0.1 g of cuprous chloride at an oil bath temperature of 92°C. The reaction was stopped after 18 hours. Isolated benzoic acid: 16 g. Distillation gave 11 g (38 %) of 2-*i*-propoxy tetrahydropyran. $n_D^{20} = 1.4253$, b.p. 43°/10 mm Hg.

Anal. $C_8H_{16}O_2$ (144.21)

Calc. C 66.63, H 11.18

Found C 66.62, H 11.19

The reaction of t-butyl perbenzoate with tetrahydropyran in the presence of t-butanol

t-Butyl perbenzoate (0.2 mole) was added dropwise to 43 g (0.5 mole) of tetrahydropyran, 0.5 mole of *t*-butanol and 0.1 g of cuprous chloride in 100 ml of anhydrous benzene, in a flask at an oil bath temperature of 95°C. After refluxing for 21 hours, the reaction was cooled to room temp., washed and dried. Precipitated benzoic acid: 18 g. Fractionation gave 12 g (38 %) of the 2-*t*-butoxy tetrahydropyran. $n_D^{20} = 1.4274$; b.p. 63°C/20 mm Hg.

Distillation residue: 16 g.

Anal. $C_9H_{18}O_2$ (158.23)

Calc. C 68.31, H 11.47

Found C 68.34, H 10.99

The reaction of t-butyl perbenzoate with tetrahydropyran in the presence of ethylene chlorohydrin

t-Butyl perbenzoate (0.2 mole) was added dropwise to 43 g (0.5 mole) of tetrahydropyran, 0.5 mole of ethylene chlorohydrin and 0.1 g cuprous chloride in 100 ml of anhydrous benzene, in a flask at an oil bath temperature of 92°C. After 18 hours, the reaction was worked up in the usual manner. 18 g of benzoic acid were precipitated. 2-(β -chloroethoxy)-tetrahydropyran was obtained at 85°C/12 mm Hg; $n_D^{20} = 1.4578$. 18 g (55 %).

Distillation residue: 9 g.

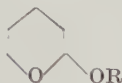
Anal. $C_7H_{13}O_2Cl$ (164.63)

Calc. C 51.07 H 7.96 Cl 21.53

Found C 51.20, H 8.05, Cl 21.32

Preparation of the 2-alkoxy tetrahydropyrans from 2,3-dihydropyran and corresponding alcohols

The reactions were performed in exactly the same manner as described for the tetrahydrofurans.



R	B.p. (°C)	mm Hg	n_D^{20}	Yield %
<i>i</i> -C ₃ H ₇	43	10	1.4255	43
<i>t</i> -C ₄ H ₉	43	10	1.4270	31
<i>n</i> -C ₆ H ₁₃	104	10	1.4391	68
Cl-CH ₂ -CH ₂	82	10	1.4577	79

SUMMARY

By reacting *t*-butyl perbenzoate with tetrahydrofuran or tetrahydropyran in the presence of catalytic amounts of cuprous chloride, 2-*t*-butoxy tetrahydrofuran and 2-*t*-butoxy tetrahydropyran respectively are formed. When an excess of an alcohol R-OH was present, the corresponding alkoxy(RO-)-derivative was isolated; possible mechanisms are discussed.

ACKNOWLEDGEMENTS

The authors wish to express their sincere gratitude to the Head of this Institute, Prof. A Fredga, for his interest in this investigation and for the facilities put at their disposal. Support from *Magnus Bergwalls stiftelse* and *Lucidol Division, Wallace and Tiernan, Inc., Buffalo, N.Y.* is gratefully acknowledged.

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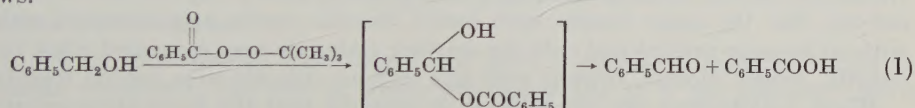
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Studies on peroxy compounds

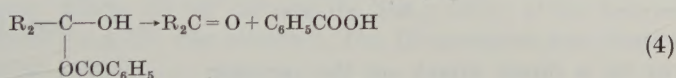
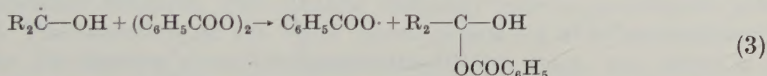
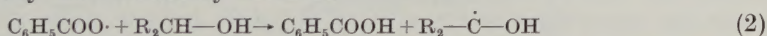
XX. The cuprous chloride catalyzed decomposition of *t*-butyl perbenzoate in alcohols¹

By SVEN-OLOV LAWESSON and CURT BERGLUND

In a recent publication [1], Sosnovsky described the reaction between *t*-butyl perbenzoate and benzyl alcohol with and without cuprous bromide present. Benzaldehyde and benzoic acid were isolated in both cases together with a higher boiling product which was not further investigated. Sosnovsky explained his findings as follows:



where a hemiacetal is an unstable intermediate. A similar mechanism has been proposed by Bartlett and Nozaki [2] for the induced decomposition of benzoyl peroxide in primary and secondary alcohols:



Gelissen and Hermans [3] had earlier observed that benzoyl peroxide in isobutanol gave aldehyde, benzoic acid, carbon dioxide and minor products.

The present authors have earlier studied the reaction between *t*-butyl perbenzoate and benzyl ether [4], in which case the dibenzylacetal of benzaldehyde was isolated; the same product was also found from the reaction between *t*-butyl perbenzoate and benzyl alcohol [5]. As we further have studied the cuprous chloride decomposition of *t*-butyl perbenzoate in ethers [6, 7] in the presence of different types of alcohols, it was felt that an investigation of the behaviour of some individual alcohols would be consistent.

In the first investigation of the reaction between *t*-butyl perbenzoate and benzyl alcohol [5] in the presence of benzene and catalytic amounts of cuprous chloride, only benzaldehyde dibenzylacetal was isolated. The reaction time was 5 h, corresponding to interruption when all perester had been consumed. Sosnovsky [1] does not give any exact reaction time for his experiment with benzyl alcohol

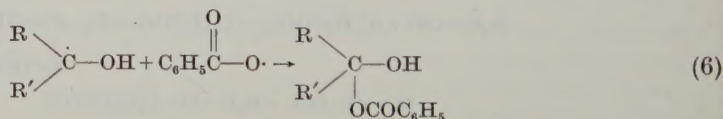
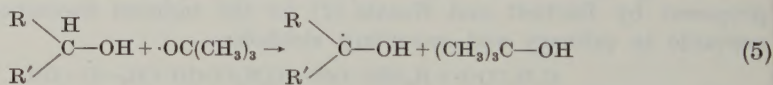
¹ Part XIX. Lawesson, S.-O. and Berglund, C., Arkiv Kemi 17, 475 (1961).

and *t*-butyl perbenzoate, but it is thought that the minimum time required for total consumption of perester would be about 3–4 h in his case. For comparison, the decomposition of benzoyl peroxide in ethyl or isopropyl alcohol occurs very rapidly, the half-life at 80°C being only 2–3 min.

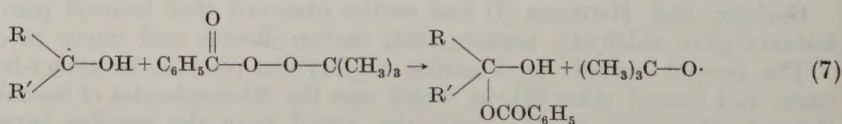
We have studied the decomposition of *t*-butyl perbenzoate in primary, secondary and tertiary alcohols in the presence of catalytic amounts of cuprous chloride, but without any solvent, and found that with primary and secondary alcohols the decomposition was rapid. No gas evolution was observed and quantitative yields of benzoic acid were found. From *n*-butanol and benzyl alcohol *n*-butyl di-*n*-butylacetal and benzaldehyde dibenzylacetal were isolated besides *n*-butyraldehyde and benzaldehyde respectively. Sec-butanol and phenyl methyl carbinol gave (as the sole products) methyl ethyl ketone and acetophenone respectively. Decomposition of *t*-butyl perbenzoate in *t*-butanol was not so rapid, some gas evolution was observed and small amounts of methyl benzoate were isolated.

In an earlier investigation we were unable to prepare benzaldehyde dibenzylacetal from benzaldehyde, benzyl alcohol and benzoic acid, but when *n*-butyraldehyde, *n*-butanol, benzoic acid and cuprous chloride now were reacted under the same conditions, a 65% yield of *n*-butyl di-*n*-butylacetal was isolated. These contradictory results made it necessary to repeat the earlier experiment with benzaldehyde, but the same results were found. Similar results were observed with and without benzene present and only the starting materials were recovered when benzaldehyde, benzyl alcohol, benzoic acid and cuprous chloride were heated together.

When α -hydrogens are available it is thought that the benzoyloxy group substitutes an α -hydrogen, thus giving a hemiacylal. This is possible in two ways:



or by a direct attack on the perester:



With primary alcohols, decomposition of the hemiacylal occurs, giving the corresponding aldehyde and benzoic acid; the formation of the acetal from benzyl alcohol may take place according to two routes: either the α -benzoyloxy ether is first formed followed by an oxygen-alkyl cleavage or the first step is the formation of the hemiacetal by an alkyl-oxygen heterolysis. At present any choice between these two alternatives is difficult. In the case of *n*-butanol, the formation of the acetal could also have started from the free aldehyde. With secondary alcohols, no ketal was formed and the decomposition of the hemiacylal was complete. Steric hindrance may be a contributing factor although a mixture of isopropanol and *n*-butanol gave no ketal.

Experimental

The reactions between *t*-butyl perbenzoate and the alcohols were carried out in an oxygen-free nitrogen atmosphere. The alcohols were distilled prior to use. *t*-Butyl perbenzoate from Light ($n_D^{20}=1.5000$) was used after drying over magnesium sulphate. The progress of the reaction was checked as follows.

The perester was dropped into the solution and at five-minute intervals a sample of the reaction mixture was taken and immediately cooled down to -70° . Using an infracord spectrophotometer, the disappearance of the perbenzoate peak at 1775 cm^{-1} was followed for the samples. When all perester had been consumed, the reaction was allowed to continue for 15 min. Boiling and melting points are uncorrected.

Starting material

n-Butanol, *sec*-butanol, *i*-propanol and benzyl alcohol were of commercial grade. Phenyl methyl carbinol was prepared by reducing acetophenone with lithium aluminium hydride [8].

Reactions of *t*-butyl perbenzoate

Reaction with n-butanol

A 500 ml three-necked flask was fitted with a stirrer, a dropping funnel and a reflux condenser, the top of which was connected to a gas collector. 250 ml (2.75 mole) of *n*-butanol and 0.1 g of cuprous chloride were placed in the flask, swept with nitrogen gas. 0.2 mole of *t*-butyl perbenzoate was added over 33 min to the alcohol solution, maintained at an oil-bath temperature of 93° . The reaction was complete after 5 min and the mixture cooled down after 20 min. The solution was diluted with ether, washed with 2 *M* NaOH and then with water, and finally dried over magnesium sulphate. The alkaline washings gave a quantitative yield of benzoic acid. Fractionation of the ether phase gave 3.3 g of *n*-butyraldehyde, identified as the 2,4 di-nitro phenyl hydrazone derivative (m.p. and mixed m.p. with an authentic sample: 122°). At $98^\circ/10\text{ mm Hg}$, 8.3 g (21%) of the butyraldehyde di-*n*-butylacetal ($n_D^{20}=1.4175$) was obtained. The IR-spectrum was identical with that of an authentic sample.

Reaction with sec-butanol

0.1 Mol of *t*-butyl perbenzoate was added dropwise over 7 min to a flask maintained at 95° , containing 100 ml (1.1 mole) of *sec*-butanol and 0.1 g of cuprous chloride. The reaction was complete after 15 min and the mixture cooled to room temperature after another 15 min. The work-up was performed as in the previous experiment, whereby 12 g of benzoic acid was precipitated. Fractionating gave, besides *sec*-butanol, 6.9 g of methyl-ethyl ketone, at b.p. $80-85^\circ$, which was identified as the 2,4-di-nitro phenyl hydrazone (m.p. and mixed m.p. $116-117^\circ$). No acetal was formed.

Reaction with benzyl alcohol

t-Butyl perbenzoate (0.2 mole) was added dropwise over 12 min to 162 g (1.5 mole) of benzyl alcohol and 0.1 g of cuprous chloride, in a flask at an oil-bath temperature of 95°C . The perester had been consumed after 10 min and after 13 min the reaction was interrupted and cooled to room temperature. The work-up

was performed as above and 24 g of benzoic acid was precipitated. Distillation gave 8.8 g of benzaldehyde, which was identified as the 2,4-di-nitro phenyl hydrazone (m.p. 235–237), and 15 g of benzaldehyde di-benzylacetal, b.p. 170/0,15 mm Hg, $n_D^{20} = 1.5778$. The IR-spectrum was identical to that of same acetal prepared from benzyl alcohol, benzaldehyde and hydrochloric acid.

Reaction with phenyl methyl carbinole

0.1 Mole of *t*-butyl perbenzoate were added over an 18 min interval to 93 g (0.76 mole) of phenyl methyl carbinole and 0.1 g of cuprous chloride. The oil-bath temperature was 96°. The solution was free from perester after 15 min and the mixture cooled to room temperature after another 15 min. The alkaline washings gave 12 g of benzoic acid. Fractionation gave, besides the carbinole, only 9.1 g of acetophenone b.p. –80–100°/10 mm Hg which was identified as the 2,4-dinitrophenyl hydrazone (m.p. and mixed m.p. 248–250°).

*Reaction with *t*-butanol*

0.1 Mole of *t*-butyl perbenzoate was added over 22 min to 1 mole of *t*-butanol and 0.1 g of cuprous chloride maintained at 92°C. The reaction time was 9 h. Certain gas-evolution was observed. A quantitative yield of benzoic acid was obtained. Fractionation gave, besides *t*-butanol, only 0.9 g of methyl benzoate ($n_D^{20} = 1.5187$) at 95–100°/10 mm Hg.

SUMMARY

Cuprous chloride decomposition of *t*-butyl perbenzoate in the presence of *n*-butanol or benzyl alcohol is a fast reaction and the products isolated are *n*-butyraldehyde + *n*-butyraldehyde di-*n*-butylacetal and benzaldehyde + benzaldehyde di-benzylacetal respectively. A mechanism is postulated which would account for the isolated products. In the case of secondary alcohols only ketones are found. The decomposition of *t*-butyl perbenzoate in *t*-butanol gives small amounts of methyl benzoate.

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